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PHYSIOLOGY OF THE CORPUS LUTEUM*

THE COMPARATIVE ACTIONS OF CRYSTALLINE PROGESTIN AND CRUDE PROGESTIN ON UTERINE MOTILITY IN UNANESTHETIZED RABBITS

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IN A PREVIOUS paper (Reynolds and Allen, 1932) we showed that corpus luteum extracts containing impure progestin inhibit spontaneous estrus uterine motility in the unanesthetized rabbit, and that similar extracts will inhibit the motility which follows the intravenous injection of theelin. These results were but part of a series of experiments (see Reynolds and Allen, 1932) demonstrating the rôle of estrin in the induction of uterine motility and that of the corpus luteum in the inhibition of such motility. These experiments showed that suitable corpus luteum extracts would inhibit estrous motility in the same manner as the corpus luteum itself. We were unable to say at that time, however, whether the inhibiting principle was identical with the hormone causing progestational proliferation of the endometrium (progestin), or whether a separate active principle was involved because no attempt was made to study any fractions except those known to contain progestin.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

We also found that inhibition of estrous motility could be obtained in the absence of proliferation if pseudopregnant rabbits were given 200 rat units of estrin per day for the first five days after mating. Under these circumstances proliferation failed to occur, presumably because of the large amount of estrin being injected even though healthy appearing corpora lutea were present in the ovaries, and at the same time the uterus became quiescent. These results could, of course, be used as evidence favoring two hormones, one causing proliferation (progestin), and another bringing about uterine quiescence. However, the motility-inhibiting factor was shown to be destroyed by treatment with alkali, in this respect being similar to crude progestin.

Considerable evidence of another type having a bearing on the possibility of a second corpus luteum hormone has appeared from several laboratories, all based on Knaus' (1930) original observation that progestin or at least corpus luteum extracts made by the method of Corner and Allen (1929), and known to contain progestin, cause inhibition of the response of the uterus to pituitrin in vitro. Knaus made no attempt to determine by quantitative analysis of the various fractions whether nonprogestin-containing fractions might contain the pituitrin-inhibiting substance to the exclusion of progestin, but work by Robson and Illingworth (1931), Tausk, de Fremery, and Luchs (1931), Fevold and Hisaw (1932) shows that such fractions can be prepared. The first two groups of workers were able by distributions between suitable solvents to get an apparent separation of two principles, and Fevold and Hisaw found that their active progestin-containing crystals had no pituitrin-inhibiting capacity. Further evidence for two hormones is to be found in experiments of another type by Robson. He (1932 *a, b*) has shown that when daily injections of anterior lobe tissue are given to female rabbits for several days, corpora lutea are formed and progestational proliferation takes place as would be expected, but curiously enough the uterus does not become refractory to pituitrin, and vice versa, that occasionally after prolonged administration a dissociation may occur in which pituitrin inhibition occurs in the absence of proliferation. It should be added that this dissociation does not occur when a single injection of anterior pituitary extract or pregnancy urine is given.

From the above considerations, it is apparent that pituitrin inhibition in vitro and motility inhibition in vivo may not be due to progestin but rather to a second corpus luteum hormone (called *desensin* by Tausk). Consequently a joint research was made by Tausk and Reynolds, studying the effects of the same fractions by both methods to see if pituitrin-inhibiting fractions which did not have good proliferating capacity would inhibit in vivo motility and vice versa (Tausk, de

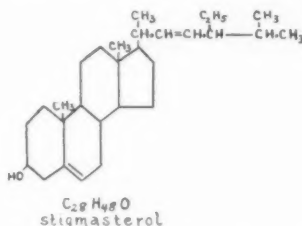
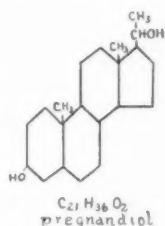
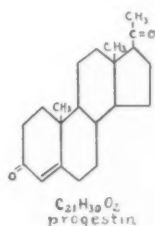
Fremery, Luchs, and Reynolds, 1934). The results were inconclusive in that both fractions inhibited spontaneous motility *in vivo*. It was evident, therefore, that proof of two distinct hormones was not forthcoming from these experiments and that more conclusive evidence would probably have to await the isolation of pure progesterin or pure desensin. Now that crystalline progesterin has become available,* answers to these questions can be expected.

In this paper we shall make a comparison of the effects of the two forms of crystalline progesterin with each other and with less pure progesterin as determined by their capacity to suppress the estrous type of motility *in vivo*.

EXPERIMENTAL

Extracts.—The crystalline preparations were made by methods similar to those recently published (Wintersteiner and Allen, 1934). The details need not be given here. The preparation designated in the subsequent experiments as 104-B was made up of 4.43 mg. of the B type, a pulverized sample of which melted at 123° to 125.5°, and which had an elementary constitution of C, 80.16 per cent and H, 9.68 per cent (theoretical for $C_{21}H_{30}O_2$, H 9.62 per cent). These crystals were not quite pure because after several more crystallizations the melting point was 127° to 128°. Such recrystallization did not appreciably alter the combustion figures or the physiologic activity. The preparation designated as 110-C consisted of 4.70 mg. of C-type crystals which melted at 120.5° to 121° and which had an elementary constitution of C, 79.58, H, 9.85.† These can be considered practically pure. The first compound (104-B) gave ++++ proliferation with 1.33 mg., ++ with 0.88 mg., and + with 0.44 mg., and the second compound ++++ with 1.28 mg., ++ with 0.94 mg., and + with 0.63 mg. when assayed by the Corner-Allen method (Corner and Allen, 1929; Allen, 1930). We considered 1.33 mg. and 1.28 mg. as a rabbit unit, respectively. For the impure progesterin we deliberately chose one of the fractions

*Recently progesterin has been isolated in pure form (Wintersteiner and Allen, 1934; Slotta, Ruschig and Fels, 1934; Butenandt, Westphal, and Holweg, 1934; Hartmann and Wettstein, 1934.) It occurs in two crystal forms: one, long needles melting at 120° to 121° and the other, short, blunt prisms melting at 128°. Both forms have the same physiologic activity as determined by their capacity to produce progestational proliferation in the rabbit. The hormone itself is an unsaturated diketone, $C_{21}H_{30}O_2$, which absorbs ultraviolet with a maximum at 240 μ . It is closely related to pregnandiol ($C_{21}H_{36}O_2$) and has been prepared synthetically from this compound, (Butenandt and Schmidt, 1934) and from stigmasterol (Fernholz, 1934.). These observations indicate without much question that the formula suggested by Slotta, Ruschig, and Fels (1934), and Butenandt, Westphal, and Cobler (1934) is correct.



†It will be noted that the combustion figures for this type show a little less carbon than the B type. This has been a more or less consistent finding and probably indicates incomplete combustion of the carbon.

We wish to express our gratitude to Dr. O. Wintersteiner for the separation of these two crystalline compounds by fractional crystallization and for the microanalyses. Without his generous cooperation, this paper would have been impossible at the present time.

which is usually discarded (or set aside) in the preparation of crystals, because it contains very little progestin but a relatively large amount of solids. Such a fraction is obtained when a moderately pure extract is distributed between 70 per cent ethyl alcohol and petroleum ether. The preparation designated as 104-K was prepared by shaking a petroleum ether solution of the hormone several times with 70 per cent ethyl alcohol, the petroleum ether fraction being used for the impure fraction (104-K) and the 70 per cent fraction (which contained most of the hormone) being further purified. This fraction contained 43 mg. of solids per rabbit unit.

Rabbits.—The rabbits used were of chinchilla or albino stock, weighing 2.8 kg. \pm 200 gm. whose sexual maturity was proved either by impregnation following mating, or ovulation after a single intravenous injection of pregnancy urine. In the first two groups of experiments recounted below (104-K and 104-B), the animals were used from one to three weeks *postpartum*, a uterine fistula being prepared (for method, see Reynolds and Friedman, 1930), and bilateral oophorectomy being done from three to six days prior to the actual experiments. The rabbits used in the study of 110-C were, for convenience, prepared in a slightly different manner. They were injected intravenously with 10 c.c. of human pregnancy urine and the fistulas pre-

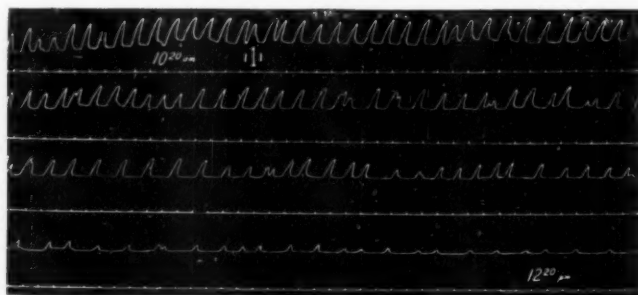


Fig. 1.—Inhibiting action on *in vivo* uterine motility of 0.6 rabbit unit (25.8 mg.) of impure progestin-containing corpus luteum extract. Extract given at 1. Inhibition of motility in slightly less than two hours.

pared and bilateral oophorectomies done six to eight days later, the motility experiments being done four to seven days after these operations. Records of uterine contractions in all cases were obtained by the use of a small intrauterine balloon connected to a Brodie bellows through an air-water system in such a way that the balloon was under virtually uniform distending tension (20 cm. water) (technic, Reynolds, 1930; Reynolds and Friedman, 1930).

Experimental Procedure.—The experimental procedure was as follows: on the day before a test, 100 R.U. of theelin* were administered in three divided doses, half intravenously and half subcutaneously. Such injections faithfully induce rhythmic uterine contractions which attain a maximum in twenty-four hours (Reynolds, 1931). This motility supplied a fairly standard background against which the inhibiting action of the extracts might be shown. The next day the balloon was inserted for twenty to thirty minutes before actual recording was begun, to allow time for subsidence of the disturbing effect attendant upon securing the animal to a board and recording. The drum was then started and after sufficient time had elapsed to show the degree of uniformity in the type of contractions, the desired amount of progestin, measured in rabbit units and diluted to one cubic centimeter with saline, was sub-

*We are indebted to Parke, Davis, and Company for the theelin used.

cutaneously injected in the left lower quadrant. A continuous record was made following the injection until there was complete inhibition of motility (Figs. 1 and 3) or until the character of the contractions had become undulating or arrhythmic (Fig. 2). The absolute end point was not always easy to determine and in some cases a certain amount of arbitrary judgment had to be employed. When the uterus becomes virtually quiescent, as in Figs. 1 and 3, there is little doubt as to when the minimum motility has been reached. Occasionally, however, all rhythmicity is lost, but long

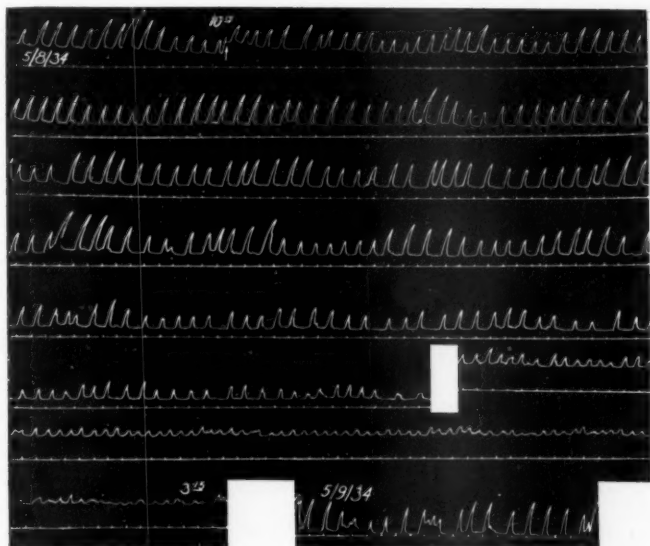


Fig. 2.—Inhibiting action of 0.2 rabbit unit (0.26 mg.) of crystalline progesterin B (m.p. 127° – 128°) on in vivo motility. Progesterin injected at 10:15. Inhibition was obtained in five hours. The arrow indicates a slight shift in the position of the rabbit, with a temporary elevation from the base line. The interruption in the sixth line indicates when the rabbit struggled loose after more than four hours of recording. The balloon was promptly replaced and the recording continued. Note that the inhibition was temporary, since motility was resumed by the next day, May 9.

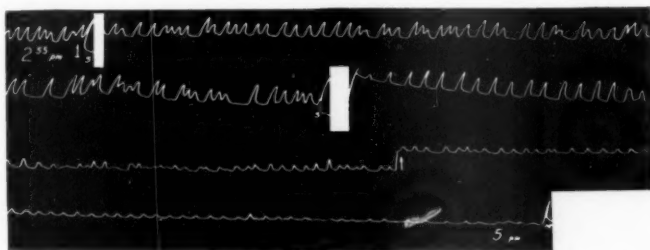


Fig. 3.—Inhibiting action of 0.6 rabbit unit (0.77 mg.) of crystalline progesterin C (m.p. 120° – 121.5°) on uterine motility. Progesterin given at 1. Rabbit struggled loose at S and again at S in the next line. The balloon was promptly replaced each time. Inhibition occurred in two hours.

uneven contractions of variable duration persist. In such cases it is our practice to continue the record for an indefinite period, to make certain that the motility will not become less within a reasonable length of time and then, if such irregular motility persists, the end point or inhibition time is considered to be the time of the onset of the disordered activity. Data from such experiments give inhibition times which correspond very well with those observations in which quiescence supervenes.

In a number of experiments records were obtained the day following the experimental procedures. At this time it was invariably observed that the small amounts of progestin used in these experiments did not prevent a return to estrous rhythm within twenty-four hours (Fig. 2).

RESULTS

Experiments carried out along the lines laid down above yielded the following results:

Crude Progestin-Containing Extract (104-K).—Of 32 experiments conducted after a number of preliminary trials, 14 were performed with the use of 0.3 Rb.U. of progestin, 15 with 0.6 Rb.U., and 3 with 1.2 Rb.U. The results are represented graphically in Fig. 4. There it may be seen that the average inhibition times for the three doses, respectively, correspond inversely to the dosage employed. The average for 1.2 Rb.U. is just under an hour; for half this dose, a little over two

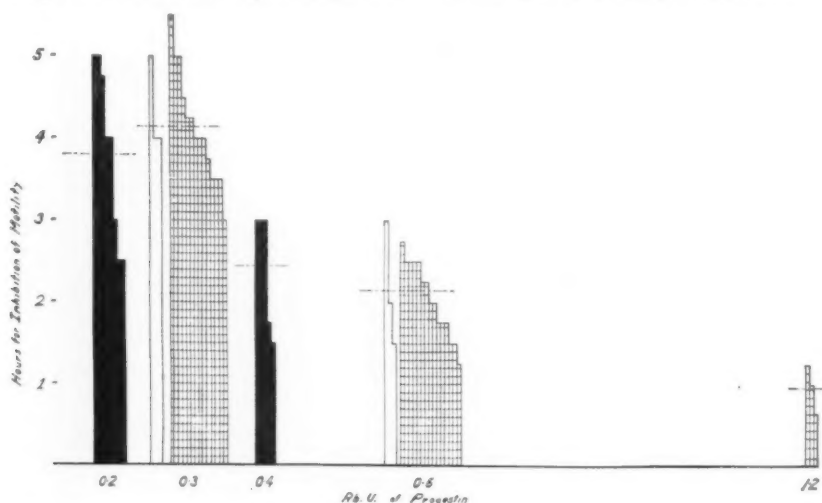


Fig. 4.—Composite chart showing the individual inhibition times in all experiments with each preparation. Solid black, crystalline progestin B; white, crystalline progestin C; latticed, crude progestin. The transverse line through each column represents the average inhibition time for each group, respectively.

0.2 rabbit unit progestin B, 8 rabbits; 0.3 rabbit unit progestin C, 3 rabbits; 0.3 rabbit unit crude progestin, 14 rabbits; 0.4 rabbit unit progestin B, 5 rabbits; 0.6 rabbit unit progestin C, 3 rabbits; 0.6 rabbit unit crude progestin, 15 rabbits; 1.2 rabbit units crude progestin, 3 rabbits.

hours, and for one-fourth the larger amount, the inhibition time is slightly over four hours. That is to say, as far as average times are concerned, one-fourth the maximal dosage requires four times as long as the maximal dosage to effect inhibition of the rhythmic contractions brought on by estrin. A glance at Fig. 4, however, reveals that this is true only when one speaks of average times, owing to the range of inhibition times within each group.

Inasmuch as the injections were made by dilution of an alcoholic solution of the hormone it was deemed advisable to determine the effect of alcohol on the time required for inhibition. The largest dose of progestin given, 1.2 Rb.U., contained four times as much alcohol as the smallest amount, 0.3 Rb.U. (ca. 0.6 c.c. of alcohol in the former and 0.15 c.c. in the latter). Therefore experiments were carried out to test the effect of the various amounts of alcohol used. Two animals were each given 0.6 c.c. of alcohol, and in each case the preinjection motility continued un-

altered for four to five hours, the period of observation. Another animal was given 0.15 c.c. of 104-K in combination with 0.45 c.c. of alcohol, thereby receiving the smallest dose of hormone (0.3 Rb.U.) given in the regular series, but at the same time a quantity of alcohol equal to that given to the animals getting 1.2 Rb.U. The inhibition time was four hours, i.e., the same as for those getting 0.3 Rb.U. in 0.15 c.c. alcohol. A fourth animal was injected with 0.3 c.c. (0.6 Rb.U.) of the extract plus 0.3 c.c. of alcohol, and in this case the inhibition time was two and one-fourth hours. It is evident, therefore, that alcohol per se does not cause inhibition of motility, and that the doses given have no effect on the time required for the development of quiescence when graded amounts of hormone are injected.

Crystalline Progesterin B (104-B, mp. 123.5°-125.5°).—In all, eight experiments with 0.2 Rb.U. (0.26 mg.) each and five with 0.4 Rb.U. (0.53 mg.) each were performed. As may be seen in Fig. 2 and in the chart, Fig. 4, inhibition of rhythmic uterine motility occurred with this form of the pure hormone. The average inhibition times were found to be, as shown in Fig. 4, nearly four hours for 0.2 Rb.U. and just under two hours and a half for the 0.4 Rb.U. dosage. The extent of the range of variation of inhibition times in both of these groups is no greater than the range of variation in the 0.3 Rb.U. series in which crude extract (104-K) was used.

Crystalline Progesterin C (110-C, mp. 120.5°-121°).—Six successful experiments have been performed with the available material of this preparation, three with a dosage of 0.3 Rb.U. (0.38 mg.), and three with a dosage of 0.6 Rb.U. (0.77 mg.). A seventh experiment was attempted but due to a faulty balloon, atypical results were obtained as described below. The inhibition times for 0.3 Rb.U. were three and three-fourths hours, three and three-fourths hours, and five hours, respectively. With the higher dosage of 0.6 Rb.U., the inhibition times were one and one-half hours, two hours, and three hours.

The only experiment in which inhibition failed to occur in a total of fifty-two was one of this series. Six-tenths of a rabbit unit of preparation C was used after the control period had shown marked uterine motility. When the injection was made, the rabbit struggled loose and broke the balloon at the same time. This was replaced and the experiment continued. As time passed, the contractions became greater and greater. The peak of the contractions did not become elevated, but the increase in amplitude continued progressively over a period of nearly five hours at the expense of the base level, as the tone diminished. When the experiment was terminated, it was found that the new balloon had become weakened on one side and was distended so that the capacity was increased to several times its normal size. Evidently, as in certain other physiologic systems (e.g., the heart), the increase in volume of the bolus within the uterus and consequent lengthening of the muscle fibers increases the irritability of the uterus and at the same time greatly enhances the efficiency of the otherwise weakened contractions.

SUMMARY

The injection of varying doses of either form of crystalline progesterin or of a partially purified progesterin fraction into castrated rabbits in which the estrous type of uterine motility has been induced by the injection of theelin causes cessation of all rhythmic contractions, as recorded without anesthesia by an intrauterine balloon. Graded injections (0.3 Rb.U., 0.6 Rb.U., 1.2 Rb.U.) of impure progesterin cause inhibition of motility in four hours (± 1 hour), two hours (± 45 minutes), and

fifty-five minutes (± 15 minutes), respectively. Crystalline progestin B, with doses of 0.2 Rb.U. and 0.4 Rb.U., and crystalline progestin C, with 0.3 Rb.U., and 0.6 Rb.U., bring about cessation of motility in approximately the same time as similar doses of the impure preparation.

DISCUSSION

It is clear that the foregoing results obtained with the use of crystalline progestin bear conclusively upon the problem of the possible diversity of action of various progestin fractions. They show, for example, that crystalline progestin in either the B or C form inhibits estrin-induced rhythmic contractions of the uterus in the castrated rabbit. Moreover, the data show that not only are both forms of progestin endowed with the inhibitory function, but when progestin-containing extracts are increasingly purified, there occurs simultaneously a proportionate increase in concentration of the hormone responsible for inhibition of motility. Thus we are forced to the conclusion that *the two hormonal effects, endometrial proliferation* (already shown to be produced by either form of crystalline progestin, Wintersteiner and Allen, 1934) *and inhibition of estrous motility, are attributable to the single hormone, progestin.* On the other hand, the results do not answer the question of whether inhibition of pituitrin responses of the uterus in vitro is due to progestin or a second hormone. Solution of that problem will have to await actual experiments, using crystalline progestin.

When this work was undertaken, the thought was entertained that the uterine fistula technic might lend itself to standardization of progestin preparations. The variation of inhibition times for the respective dosages with no sharp delineation between the shortest inhibition time of one group and the longest inhibition of the next group renders this method inapplicable, however. With unknown dosages this would present a serious difficulty. Still another objection to the fistula method lies in the fact that substances other than progestin inhibit estrous motility (prolan and certain anterior pituitary extracts, Reynolds, 1932a; 1932b). Unless one knows, therefore, that pure progestin is being used, one cannot rely upon inhibition alone as a test for progestin. Accordingly these and other considerations make it obvious that the preferred biologic method for standardization of progestin continues to be the Corner-Allen method of histologic assay.

These experiments, together with those which we have reported previously, using crude progestin-containing extracts (Reynolds and Allen, 1932), provide the scientific basis for the suggested use of progestin in certain forms of dysmenorrhea. Its possible use in this condition is very attractive; strong uterine contractions, which in laboratory animals are known to occur only when under the influence of estrin, presumably

account for the crampy pain of severe dysmenorrhea in some instances; assuming that these contractions are due to estrin, the same as in rabbits, progestin would be expected to alleviate the symptoms. The dose necessary should not be great; in fact it should of necessity be less than the amount necessary to produce a premenstrual endometrium, since the injection of such an amount would probably delay the onset of the menstrual period rather than alleviate the cramps. That such a possibility is a real one is shown by experiments in monkeys in which progestin is known to delay an experimentally induced menstrual period (Smith and Engle, 1932) as well as a normal period (Corner, 1935). Some basis for this opinion regarding dosage is found in our own experiments with rabbits: a single subcutaneous injection of 0.2 rabbit unit will bring about complete quiescence in about five and one-half hours while a similar dose must be given for five days to bring about full progestational growth of the endometrium (Reynolds and Allen, 1932). The exact amount necessary for human use cannot, of course, be deduced from these experiments, but one would not expect it to be great when we consider the fact that Kaufmann (1933) has produced a premenstrual endometrium with from 35 to 90 rabbit units. The fact that crystalline progestin ($C_{21}H_{30}O_2$) causes this inhibition of motility in a manner identical with crude extracts has considerable clinical bearing also, because the hormone will probably be supplied in the synthetic form rather than in the naturally occurring form.

The use of progestin in other conditions such as habitual and threatened abortion, premature labor, and hyperplasia of the endometrium seems less certain of success but nevertheless worthy of trial (see Krohn, Falls, and Lackner, 1935). In abortions, many times, the termination of the pregnancy is secondary to an abnormal embryo, but there are in all probability some cases in which the abortion is due to an exceptionally irritable uterine muscle; in such cases and in premature labor, not associated with mechanical defects such as rupture of the membranes, progestin might be beneficial. Its suggested use in hyperplasia is based on the well-known observation that in most cases this condition is associated with absence of corpora lutea.

CONCLUSIONS

Purification and concentration of impure progestin-containing extracts of corpora lutea, with ultimate crystallization of progestin, are accompanied by a simultaneous and proportionate increase in the two hormonal effects, endometrial proliferation and inhibition of uterine motility in unanesthetized rabbits. It is evident, therefore, that these are dual properties of the single hormone, progestin.

The bearing of this work on certain clinical problems is discussed.

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NOTE: In a recent note in *Science* (Vol. 82, No. 2120, page 153), signed by W. M. Allen, A. Butenandt, G. W. Corner and K. H. Slotta, (the newly adopted name for the corpus luteum hormone is given as *progesterone*.) Heretofore it has been known as *progestin* (Wintersteiner and Allen) and *luteosterone* (Slotta et al.). In this paper the B-type crystals of *progestin* (on p. 1280) are known now as *A progesterone*, and the C-type crystals of *progestin* (on p. 120, 5°-121°) are now known as *B progesterone*.

CANCER OF THE FEMALE URETHRA*

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THE relative scarcity of primary carcinoma of the female urethra justifies this report of 22 cases. Counseller and Paterson,¹ reviewing the literature in 1933, found a total of 136 cases, including 12 of their own. Two cases reported by Fukai and Yoshida² are not included in their summary. Benson³ reported a case in 1932. Mercur and Grenier⁴ reported a case in 1933, as did Eichenberg⁵ and Muller,⁶ respectively. Pomeroy⁷ reported 3 additional cases in 1934. The 22 cases, which are included in this report, bring the total number of cases found in the literature to 167. Were this figure a true one, carcinoma of the female urethra would indeed be a rarity. However, many times this number of patients probably have been treated, but have gone unreported.

*Read at a meeting of the St. Louis Gynecological Society, May 10, 1935.

Eighteen of these patients were seen at the Barnard Free Skin and Cancer Hospital, on the services of Drs. G. Gellhorn and F. J. Taussig. The other 4 patients were seen and treated by these 2 men in their private practice. Fifteen cases were seen more than five years ago. The balance were seen during the years from 1930 to 1934. Of the 15 patients seen before 1930, 2 refused treatment, 8 are dead, and 5 survived the five-year period. The 2 patients who refused treatment were not followed by the social service department, so that their fate is unknown. Six of the 7 patients treated within the past five years remain alive and apparently well, periods varying from a few months to almost five years.

The average age of these patients was fifty-four. The youngest was thirty-nine and the oldest seventy-five. This high average age is in accordance with the figures quoted by various other authors. All of these patients were married, but this fact is of academic interest, rather than of significant value, because approximately 95 per cent of all the patients examined in our clinic are or have been married. Ninety-two per cent of all the patients examined have borne children, so that the question of parity in our patients with urethral cancer is of no consequence in relation to etiology. The figures mentioned relate only to white women, as no colored women were seen with urethral cancer. Urethral caruncle has preceded the cancer in several of these cases. It is the only concrete evidence that could possibly be taken as a predisposing factor.

The point of origin for cancer of the female urethra is probably on the posterior wall at or near the external urinary meatus. In practically all of the early cases this was the area involved. In the more advanced cases the posterior urethral wall was always invaded; whereas, the anterior wall sometimes was found free of cancerous invasion. So far as can be ascertained, the middle and posterior third of the urethra have never been the primary site of the neoplasm.

The chief complaint of the patients was pain and burning on urination. Frequency of urination was the next complaint in order of frequency. Practically all of the advanced cases gave one of these symptoms as their earliest complaint, although at the time that they presented themselves for examination, other symptoms, such as bleeding, swelling, or local growth were noted. There was one case of acute urinary retention prior to treatment.

In this series there was a great predominance of squamous cell carcinoma. There was one primary melanoma and two adenocarcinomas. The former is an extremely rare lesion, only three or four having previously been reported. However, Dr. Q. U. Newell⁸ of this city, treated another woman with melanoma of the urethra at about this same time. His patient is still alive about two and a half years after treatment. A complete report of this extremely rare lesion and a review of the literature will soon be made available by him.

Treatment of these cases has consisted of local excision or local radiation, with small, well-screened doses of radium. Radium is best used in the form of emanations, in either gold or platinum seeds. If this form of radiation is unavailable, 25 to 50 mg. of radium element, screened in the equivalent of 1.25 mm. of platinum, surrounded by rubber sewed into the urethral canal at the site of the lesion, should be used. We have employed from 400 mg. hours to 4,100 mg. hours in the local treatment of urethral carcinoma, the amount depending entirely on the size of the local lesion. No arbitrary dosage of radium can be prescribed, as radium dosage is entirely a matter of experience. Despite the large amount of tissue damage resulting from some of the radiation, only two patients had incontinence of urine.

In certain instances radical surgical removal of the regional lymphatics, both above and below the inguinal ligament (Basset operation)⁹ was done in addition or in combination with the local treatment. X-ray therapy was used as a palliative measure in three cases. We do not believe that x-ray therapy is efficacious in the treatment of the local lesion, or of glandular metastases. Therefore, it was not used as a therapeutic agent.

The age and physical condition of the patient, the extent of the local lesion, and the presence of palpable inguinal glands were factors in the decision as to the method of choice in the treatment of any individual case. Every cancer patient, regardless of the location of the lesion, must be considered individually, and no single treatment should be advocated to cover a group of patients with the same lesion. In this series of cases no patient of extreme age was subjected to a radical surgical procedure. Neither was this operation used in patients who were obviously in a hopeless condition. Therefore, only early and moderately advanced cases were primarily considered as being suitable for radical surgery in addition to local treatment of the urethral cancer.

The Basset operation is a comparatively safe surgical procedure. The operative mortality is low when the patient's general condition is good. The lymphatic drainage of the female urethra is similar to that of the vulva, and this same operation has produced excellent results in the hands of Taussig¹⁰ who has reported 63 per cent five-year cures in a large series of vulvar carcinoma. Six Basset operations were performed in this series of cases with no mortality. Neither has there been a recurrence of cancer in any of these patients. In one case, the melanoma, it was impossible to clear up the local condition, and metastases to the bladder and other parts of the body caused death in one year.

We now believe that the Basset operation, combined with local radiation, is the treatment of choice in all early and moderately advanced cases of cancer of the female urethra, if in the judgment of the operator the patient is a fairly good operative risk. The small size of a local lesion that has proved to be cancer by microscopic examination should never

influence one toward conservatism in the treatment of this condition, for metastases have been found in the regional lymph nodes with an extremely small primary lesion. Conversely only hyperplastic nodes have been found with relatively far-advanced local lesions. It seems quite evident that carcinoma of apparently the same type and grade metastasizes in different individuals differently according to some unknown characteristic. We agree with Mikulicz¹¹ in his belief that a third of all cases of cancer with this same lymphatic drainage have regional lymphatic metastases. It is only by operation that these patients with glandular metastases have a chance of ultimate survival. In our hands the use of x-ray on lymphatic metastases has been very disappointing, if not entirely without merit.

TABLE I

TREATMENT	NUMBER	DIED	CURES LIVED MORE THAN 5 YEARS	LIVING AND WELL LESS THAN 5 YEARS
Local, only	14	8	2	4
Local plus Basset operation	6	1	3	2
No treatment	2	2	0	0
Total	22	11	5	6

Summarizing the Results of Treatment: Nine early cases were seen. Two patients refused treatment. Six had only local treatment, and one had local treatment plus a Basset operation. Two of the three early cases treated more than five years ago lived more than five years. The third died of metastases four years after local excision. This case emphasizes the necessity for gland removal in the earliest cases. Of the four more recent cases, one had a cautery excision more than three years ago. Two had cautery excision followed by less than 900 mg. hours of heavily screened radium almost five years and one year ago, respectively. The fourth had radium locally followed by a Basset operation. All of these women are living and apparently free of cancer at the present time.

Five advanced cases have been treated. One patient had radium locally and is alive and well more than two years. The other four had a Basset operation in addition to local destruction of the tumor by means of cautery or radium. One is well more than two years, one is well more than five years, one is alive more than twelve years, and the fourth patient died nine years after treatment, due to cancer of the breast, which was considered a new malignancy and not a metastatic growth.

The remaining eight patients were considered hopeless when seen. All were given palliative radiation, except one, who had a Basset operation in addition to local radiation, because of the highly malignant nature of the tumor, and with the hope that her life could possibly be prolonged. She lived one year after treatment; whereas, none of the others survived a six-month period.

The results of treatment in this small series of cases make certain conclusions logical. First, except in very far-advanced cases that are considered hopeless when seen, the prognosis is good. This is in contradiction to almost all other authors on this subject. Second, the early case of urethral cancer in the female can be successfully treated by local excision, local radiation, radical surgery, or a combination of either of the first two with the third. We strongly urge the routine use of the Basset operation in combination with local radiation as the method of choice in these early cases, as even the very early case may have already metastasized to the regional lymphatics in spite of the minuteness of the visible lesion. Third, the advanced case that is not yet hopeless is best treated by local radiation and Basset operation, as practically all of these cases will show glandular metastases. Fourth, the very far-advanced case that is practically hopeless when first seen should receive only palliative treatment and as much relief from terminal pain as is possible.

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1045 MISSOURI THEATER BUILDING

Rose, D. K.: Postpartum Pyelitis of Pregnancy, *Am. J. Surg.* 25: 394, 1934.

In postpartum pyelonephritis with bladder retention in which catheter interference is indicated either from dysuria or toxicity, two entirely opposite types of bladder function are encountered. Either may exist separately, or the two may coexist to any degree.

The postpartum bladder showing a relatively fixed, compensated bladder wall back of a physiologic block of the external sphincter, if of sufficient degree, requires continuous drainage when indicated by reason of infection. Such drainage primarily reduces bladder infection and, secondarily, urethral, pelvic and kidney infection by facilitating ureteral flow by a decompressed and perfectly drained bladder. Intermittent catheterization in such a bladder traumatizes in the presence of imperfect drainage and tends to generalize the infection. Irritative instillations in such bladders are contraindicated.

If sufficient degree of altered bladder function occurs, continuous bladder drainage is indicated until perfect function is restored.

The postoperative bladder with inhibited or functionally weakened bladder wall and with normal sphincter tone requires only intermittent catheterization. Irritating instillations in these bladders may be of value.

J. THORNWELL WITHERSPOON.

BLOOD LIPIDS IN ECLAMPSIA

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BLOOD lipids have been determined in eclampsia on several occasions. Cholesterol, being the most readily estimated, has received the greatest amount of attention. Serum cholesterol was reported in three cases of eclampsia in 1911 by Chauffard, Laroche and Grigaut¹³ who found no consistent variation from the concentration in the serum of healthy gravidas. A similar conclusion may be drawn from a collective survey of subsequent work on blood cholesterol.^{1, 12, 14, 17, 21, 23}

A differential analysis of all or nearly all of the blood lipids in eclampsia has been made in whole blood by Lindemann¹⁸ and by Slemons and Stander²⁴ and on serum by Hellmuth.¹⁶ Lindemann¹⁸ has presented the largest series of cases and his results, although determined over twenty years ago with a less refined technic than is possible now, bear many points of similarity to those recorded below. He concluded that blood lipoids were elevated in eclampsia and the "fat" low; analysis of his results reveals that he got an increase in the phospholipid to cholesterol ratio. Slemons and Stander²⁴ concluded that there was no significant change in the concentration of any lipid in whole blood but again four of their six cases may be seen to have had a phospholipid cholesterol ratio higher than their average for normal pregnancy. Hellmuth¹⁶ reported four cases, none showing any marked changes in serum lipids.

It became obvious to the author that if any variation in the blood lipids were to be found in eclampsia, a correlative study of all the lipids in whole blood, plasma and the red blood cells would be required. This principle was apparent in a survey of blood lipids in normal gestation, in which Boyd⁶ found that the major changes occurred in plasma only and affected to different degrees the values of the several lipids. The nature and concentration of the lipids of plasma differ from those of the red blood cells and whole blood analyses are in general unsatisfactory, a fact also emphasized by Boyd in a study of the blood lipids in relation to lactation⁹ and to fever.¹⁰

The patients studied were from the Obstetrical Divisions of the Strong Memorial Hospital. When possible, blood was obtained with the patient in a fasting state; when a patient was in convulsions, blood was taken irrespectively of whether or not the patient had ingested food within fifteen hours. Recent work⁸ has cast doubt on the popular opinion that blood lipids are markedly increased in value after meals,

at least in normal persons. The lipid composition of whole blood, plasma and the red blood cells was determined by Bloor oxidative micromethods as modified by Boyd.^{3, 4, 8} The lipid content of the white blood cells was likewise determined but found to be no different from that of healthy gravidas⁷ and of nonpregnant women;⁵ hence these results have not been reported.

CHANGES IN BLOOD PLASMA

As in normal gestation, so in eclampsia the most significant changes in blood lipids occurred in plasma, the results of which are given in Table I. In this table are included values for plasma lipids in five cases of eclampsia and two cases of preeclampsia which exhibited variations similar to those found in the eclamptic cases. These latter two cases have been considered to be cases of "eclampsia without convulsions" or to belong to what has been termed the "eclamptic state." The author has examined blood from many cases of so-called preeclampsia, but only two exhibited the same changes as the convulsive patients, these being the two included in Table I. Changes in the blood lipids in the remaining noneconvulsive or "noneclamptic"

TABLE I. THE LIPID COMPOSITION OF BLOOD PLASMA IN THE ECLAMPTIC STATE. THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF PLASMA

DIAGNOSIS	TOTAL LIPID	COMPOSITION OF TOTAL LIPID					RATIO P/TC
		NEU- TRAL FAT	CHOLESTEROL			PHOS- PHO- LIPID	
			TOTAL	ESTER	FREE		
Preeclampsia	1032	309	256	172	84	352	1.38
Preeclampsia	1350	382	321	205	116	510	1.59
Intercurrent eclampsia	513	101	138	90	48	214	1.55
Antepartum eclampsia	991	408	191	118	73	314	1.64
Antepartum eclampsia	806	276	193	86	107	279	1.45
Antepartum eclampsia	987	528	138	92	46	259	1.88
Postpartum eclampsia	1445	572	277	161	116	488	1.76
Mean of eclamptic state	1018	368	216	132	84	345	1.61
Standard deviation	292	147	65	44	28	106	0.16
Standard deviation in per cent of mean	29%	40%	32%	33%	33%	31%	10%
Normal pregnancy	900	353	205	140	65	248	1.22
Mean \pm St. Dev.	± 130	± 75	± 45	± 47	± 15	± 43	± 0.12
Nonconvulsive pre- eclampsia	863	275	233	160	73	250	1.08
Mean \pm St. Dev.	± 119	± 117	± 24	± 27	± 12	± 27	± 0.10

preeclamptic patients have been found¹¹ to be entirely different from the changes in the convulsive group. For comparative purposes, means for this group and for normal pregnancy as found in previous investigations^{6, 11} have been included in Table I and, as indicated, in the remaining tables.

The mean value of each lipid was determined and the standard deviation of the mean calculated from the formula

$$\theta = \sqrt{\Sigma(\chi)^2/\eta}$$

where θ represents the standard deviation, Σ a summation symbol, χ the variation of each value from the mean and η the total number of readings. The means and standard deviations so obtained have been compared with corresponding values deduced for normal pregnancy⁶ and the nonconvulsive toxemias of pregnancy.¹¹ Statistically, the difference between two groups of values may be considered significant when the mean plus or minus the standard deviation for one group is beyond the mean plus or minus the standard deviation for the other group. This indicates that two-thirds of all values in the one group may be expected to be beyond two-thirds of all values of the second group. The mean plus or minus twice the standard deviation includes 95 per cent of all expected values for the group. The results have been submitted to this critical survey because all too frequently significant differences have been claimed on variation of means alone, which is quite inadequate.

The point is well illustrated in the present figures. Thus, the mean values of all lipids except ester cholesterol were higher in eclampsia than in normal pregnancy. Offhand one might conclude, as did Lindemann,¹⁸ that the concentration of lipids is increased in eclampsia. The standard deviations reveal that the range for eclampsia was greater than that for, and included the range of, normal pregnancy. Hence it may be concluded that there is no significant variation in the concentration of any lipid of plasma in eclampsia.

When, however, the difference between the ratio, phospholipid/total cholesterol (P/TC) is considered, a significant variation may be noted. The mean value for the ratio was 1.22 in normal pregnancy, 1.08 in the nonconvulsive toxemias and 1.61 in eclampsia. The range, mean $\pm \theta$, for eclampsia was well above the same range for normal gestation and for the nonconvulsive toxemias. Statistically it may be concluded that three-fourths of all values for the ratio in eclampsia will be above three-fourths of all values for the ratio in noneclamptic patients. Actually, the author has never found a value for the P/TC ratio above 1.40 in noneclamptic toxemias or in normal gravidas except in the two cases of preeclampsia which have been included in Table I. Both of these cases exhibited muscular twitchings in addition to the usual symptoms of preeclampsia and in view of the lipid findings, they have been grouped as literally preeclamptic.

Further evidence that the increased P/TC ratio in eclampsia is significant may be deduced from the percentage standard deviations ($\theta/\text{mean} \times 100$) given in Table I. The percentage standard deviation

for the plasma lipids varied between 29 and 40 per cent. The percentage standard deviation for the P/TC ratio was 10 per cent. This indicates that the variation of the P/TC ratio from one case to another was only one-third or one-quarter the variation in single lipid values. In other words, although the concentration of plasma lipids varies greatly in eclampsia, a fact noted by previous authors, the ratio P/TC is consistently and regularly high.

The author believes, therefore, that a high plasma P/TC ratio may be said to characterize the eclamptic state. He has tentatively selected a ratio of 1.40 as the dividing line between eclamptic and noneclamptic cases. This value may require a slight shift up or down in the light of subsequent work. The value depends also, of course, on the use of methods exactly as herein given.

CHANGES IN WHOLE BLOOD

In Table II have been given the means and standard deviation of the lipid values for whole blood in eclampsia. A survey of the values will reveal that in each case the range in eclampsia overlaps considerably

TABLE II. ILLUSTRATING THAT THE SIGNIFICANT CHANGES ENCOUNTERED IN PLASMA DO NOT APPEAR IN WHOLE BLOOD. RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF WHOLE BLOOD

DIAGNOSIS	TOTAL LIPID	COMPOSITION OF TOTAL LIPID					RATIO P/TC
		NEU- TRAL FAT	CHOLESTEROL			PHOS- PHO- LIPID	
			TOTAL	ESTER	FREE		
Mean of eclamptic state	829	219	187	90	97	361	1.96
Standard deviation	255	120	56	39	22	102	0.29
Normal pregnancy	785	248	179	95	84	293	1.66
Mean \pm St. Dev.	± 117	± 63	± 35	± 29	± 11	± 52	± 0.26

the range for normal pregnancy. A similar overlapping occurred with the P/TC ratio of whole blood. Hence it may be concluded that the significant changes encountered in plasma do not appear in whole blood. The previous studies of Lindemann¹⁸ and of Slemons and Stander²⁴ were with whole blood.

CHANGES IN THE RED BLOOD CELLS

The lipid composition of the red blood cells in eclampsia likewise was found to exhibit no significant variation from that in normal pregnancy (Table III). The noneclamptic toxemias were distinguished from the eclamptic by having considerably more neutral fat in the red blood cells. Boyd¹¹ has shown that the characteristic of these non-convulsive toxemias is an alteration of the normal equilibrium between the lipids of plasma and those of the red blood cells.

RECOVERY FROM ECLAMPSIA AND THE PLASMA P/TC RATIO

From the above survey of the lipid concentration in whole blood, plasma and the red blood cells, it was concluded that one change and one alone characterized the blood lipids in the eclamptic state, i.e., an increase in the plasma P/TC ratio. Further proof that this alteration is significant may be seen in the return to normal of the plasma P/TC ratio when the patients recovered from eclampsia. In four cases of eclampsia, the author was enabled to take samples of blood on several occasions during convulsions and recovery. Variations thus found in the plasma P/TC ratio are given in Table IV. It may be seen that as the patient improved and then recovered from the convulsive state, the ratio fell from its high value to 1.0 or lower, which is about normal. This again is evidence that the eclamptic state is associated with a high plasma P/TC ratio.

TABLE III. THE LIPID CONTENT OF THE RED BLOOD CELLS IN THE ECLAMPTIC STATE. THE RESULTS ARE EXPRESSED IN MG. PER 100 C.C. OF CELLS

DIAGNOSIS	TOTAL LIPID	COMPOSITION OF TOTAL LIPID				PHOSPHO- LIPID
		NEU- TRAL FAT	CHOLESTEROL			
			TOTAL	ESTER	FREE	
Mean of eclamptic state	638	78	146	40	106	387
Standard deviation	333	63	88	58	29	196
Normal pregnancy	594	89	133	16	121	361
Mean \pm St. Dev.	± 123	± 80	± 62	± 21	± 43	± 155
Nonconvulsive pre-eclampsia	826	246	131	7	125	458
Mean \pm St. Dev.	± 128	± 101	± 21	± 8	± 17	± 59

TABLE IV. ILLUSTRATING THAT THE ELEVATED P/TC RATIO IN THE ECLAMPTIC STATE DISAPPEARS AS THE PATIENT RECOVERS

PATIENT	DAY OF DISEASE	CLINICAL CONDITION	P/TC RATIO
R. F.	16 days antepartum	Convulsions	1.55
	9 days antepartum	No convulsions, patient apparently well	1.98
	2 days antepartum	Return of all symptoms but no convulsions; labor induced	
	1 day postpartum	Patient rapidly recovering	1.37
R. W.	1 day antepartum	Convulsions	1.64
	2 days postpartum	Improving	0.94
	9 days postpartum	Recovered	0.69
M. S.	2 days antepartum	Convulsions	1.45
	1½ days postpartum	Improving	1.24
	6 days postpartum	Recovered	1.04
	11 days postpartum	Recovered	1.13
M. W.	1 hour postpartum	Convulsions	1.76
	12 hours postpartum	Convulsions ceased	1.41
	14 days postpartum	Recovered	1.13

THE RELATION OF THE PLASMA P/TC RATIO TO CONVULSIONS

In one case of intercurrent eclampsia, patient R. F. in Table IV, lipid analyses revealed that a high ratio may be present without convul-

sions necessarily occurring. This patient had convulsions shortly after admission to hospital and at that time gave a plasma P/TC ratio of 1.55. Under a modified Stroganoff treatment she recovered and most of her symptoms disappeared. A week after the initial convulsions, lipid analysis revealed an even higher ratio, 1.98. One week later again, all her symptoms (hypertension, albuminuria, edema, etc.) suddenly returned but no convulsions occurred. Labor was induced and the patient delivered. In the second day of the puerperium she began to improve rapidly and her ratio fell immediately to 1.37. This

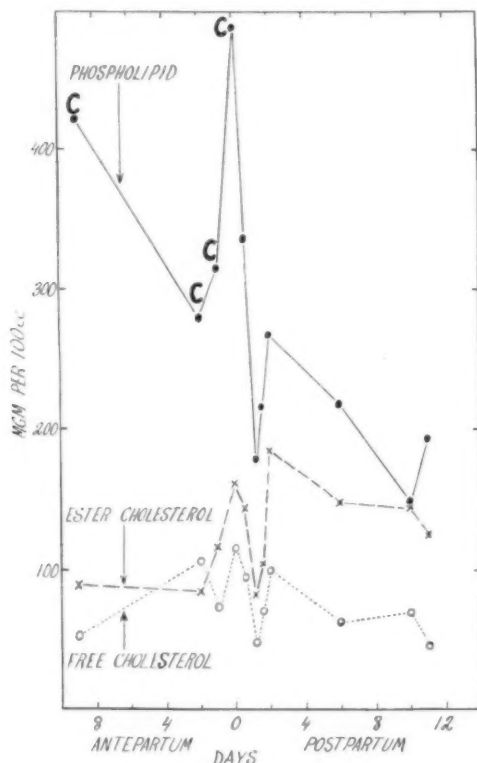


Fig. 1.—The values of plasma phospholipid, ester cholesterol and free cholesterol in relation to convulsions in, and recovery from, eclampsia. The presence of convulsions is indicated by a C.

suggests that the high ratio is not due to convulsions but to the underlying cause of the eclamptic state. The case also exhibited the value of estimating the ratio in determining the course of action to be taken in dealing with such types of eclampsia.

TO WHAT IS THE ELEVATED PLASMA P/TC RATIO DUE?

An elevation of the plasma P/TC ratio may be due to two things, (a) an increase in phospholipid or (b) a decrease in total cholesterol. The data given in Table I indicate that either one or both of these factors

may operate to increase the ratio in eclampsia. Study of the plasma lipids during recovery from eclampsia suggested that a return to normal in the ratio is due chiefly to a decrease in the concentration of phospholipid.

The puerperium of eclamptic patients was found associated with a fall in the value of plasma neutral fat and phospholipid; minor changes occurred in the cholesterol fractions and in fact ester cholesterol actually rose in value in several instances. No relation has been noted between neutral fat and eclampsia and the decreasing value of this lipid in the puerperium corresponded to the decrease found during lactation in normal puerperas.⁹ These changes have been shown graphically in Fig. 1.

In Fig. 1 there have been plotted the values for phospholipid and both cholesterol fractions, i.e., the lipids directly concerned in determining the value of the P/TC ratio. It may be seen that when the ratio returns to normal, the change is due chiefly to a decrease in the concentration of phospholipid, no change in free cholesterol and perhaps a slight increase in ester cholesterol.

SIGNIFICANCE OF THE P/TC RATIO

Mayer and his associates, especially Schaeffer and Terroine, proposed some years ago that lipid ratios (in tissues) were equally if not more important than the actual concentration of single lipids. In recent years the tendency has been to discount the importance of the lipid ratios and return to actual lipid values. From time to time, however, reports have appeared which showed that perhaps there was some significance in the ratios. Thus, McQuarrie, Bloor, Husted and Patterson¹⁹ found comparatively minor changes in the lipid composition of blood plasma of 100 epileptic children, but McQuarrie, Husted and Bloor²⁰ subsequently showed that a significant increase in the plasma P/TC ratio occurred at or about the time of convulsions in epilepsy. Two deductions may be made from this work which are of importance to the interpretation of the present data. First, the changes in the plasma P/TC ratio were found more significant than changes in the individual lipid values, exactly as herein found, and second, the plasma P/TC ratio was found highest at the time of the epileptic convulsions. Clinically the sequence of the convulsion in grand mal is almost identical with that in eclampsia. It appears probable that a similar change in body metabolism is responsible for both convulsions. This change is characterized by, and may even be due to, an elevated plasma P/TC ratio.

Considerable has been written on the antagonism between phospholipid and cholesterol, and Sinclair²² has presented a recent able review of the subject. Briefly, under normal conditions the relation between phospholipid and cholesterol both in blood and in tissues is fairly con-

stant: when one increases the other increases and vice versa. Phospholipid is hydrophilic and cholesterol is hydrophobic. Intravenous injections of large amounts of an emulsion of phospholipids increase the value of blood phospholipid and favor the retention of water by the tissues. A relative increase in blood phospholipid is apparently, therefore, accompanied by a relative increase in tissue phospholipid, thus favoring the retention of water in the tissues.

In the eclamptic state, a somewhat similar situation may be deduced from the present results. There has been shown to occur a relative increase in plasma phospholipid. It may be offered that probably this altered equilibrium between blood and tissues would result in a relative increase in tissue phospholipid, thus favoring retention of water by the tissues. There is a good deal of evidence suggesting a change of water balance in eclampsia. Clinically, the patients have a noticeably puffy appearance. Harding and Van Wyck¹⁵ found that administration of sodium chloride, which also favors retention of water in the tissues, increased all the symptoms of toxic pregnancy.

The relation of water retention to convulsions becomes more apparent if attention is confined to the tissues of the brain. Increased water retention by the brain, due, may it be offered, to an increased plasma P/TC ratio favoring increased phospholipid values in the brain, will result in increased pressure within the bony skull. When this surpasses a certain maximum, the irritability of the nerves may reach a point at which convulsions ensue. Such an explanation, deduced from the present data, is offered as a working hypothesis, not as a proved theory.

METHOD FOR DETERMINING THE PLASMA P/TC RATIO

Add 2 c.c. of plasma to 35 to 40 c.c. of alcohol ether (3:1, both redistilled), heat to boiling for two minutes on a steam bath, cool, filter through alcohol-extracted filter paper, wash with solvent, press out the precipitate, and make filtrate up to 50 c.c.

(a) *Phospholipid*: 25 c.c. of the alcohol ether extract are evaporated to dryness without overheating in tall 100 c.c. beakers. Add 2 or 3 c.c. of redistilled petroleum ether, heat to boiling, and pour off into a 15 c.c. centrifuge tube. Repeat extraction 5 times. Centrifuge. Pour supernatant solution quantitatively into 15 c.c. graduated centrifuge tube and evaporate to just below 1 c.c. Make up to 1 c.c. with petroleum ether, add 7 c.c. of dried, redistilled acetone and 0.1 c.c. of 30 per cent magnesium chloride in 95 per cent alcohol. Let stand one-half hour. Centrifuge, pour off supernatant solution and discard it (or by evaporating it and redissolving in alcohol it may be used for total cholesterol if the amount of blood is limited, in which case 1 c.c. of plasma will suffice). Dry with air and dissolve precipitate of phospholipids in 10 c.c. of moist ether with stirring. Centrifuge and transfer quantitatively to a 125 c.c. glass-stoppered Erlenmeyer flask. Evaporate off solvent and avoid overheating; remove last traces of ether vapor with a gentle stream of air. Add 3 c.c. of NiCloux reagent (prepared after Bloor²), and 5 c.c. of 1 N potassium dichromate. Heat for twenty minutes at $124 \pm 2^\circ$ C. in an oven, placing flask on a cast iron plate. Remove from oven, add 75 c.c. of ice cold distilled water,

10 c.c. of 10 per cent potassium iodide and titrate with 0.1 N sodium thiosulphate, using 1 per cent starch solution as an indicator. Subtract the value obtained from that of a blank containing only the oxidizing agents and heated as the unknown, divide the difference by 3 and multiply by 100 which gives the mg. of phospholipid per 100 c.c. of plasma. All glassware must be cleaned with chromic acid cleaning solution, thoroughly rinsed with distilled water and dried. All the solvents must be redistilled and free of organic matter, the ether being also peroxide free.

(b) *Total Cholesterol*: The author has recently described the method for the microestimation of total cholesterol using digitonin precipitation followed by oxidation as with phospholipid⁴ to which may be added certain precautions and minor modifications later found.⁵ By these procedures the concentration of total cholesterol in milligram per cent is found. The value of the phospholipid total cholesterol ratio is then found by dividing the phospholipid value by that for total cholesterol. For further details of method, previous papers by the author may be referred to^{3, 6, 7, 8} as well as references to the work of Bloor, Okey, Yasuda, etc., therein contained.

SUMMARY

In order to ascertain if there were any *significant* changes in the blood lipids in eclampsia, a quantitative estimation of *all* lipids in whole blood, plasma, the red blood cells and the white blood cells was made. It was found that the concentration of lipids varied greatly in eclamptic patients but no significant variation occurred in the value of any *single* lipid.

The ratio of phospholipid to cholesterol in plasma was found, however, to be without exception higher in eclampsia than in other toxemias or in normal gestation. The mean minus the standard deviation for the ratio in eclampsia was higher than the mean plus the standard deviation in normal gravidas and other toxemias. Variations in the value of the ratio from one eclamptic patient to another were only one-third to one-fourth as great as the variation in single lipids, indicating that the ratio was also less variable than the component lipids.

When the patients recovered from eclampsia, the ratio P/TC of plasma returned quickly to normal due chiefly to a fall in the value of phospholipid.

Cessation of convulsions without termination of pregnancy left the ratio still high, indicating that a high ratio did not result from convulsions but was associated with and possibly accounted for the eclamptic state.

Only a small proportion of cases diagnosed as preeclampsia were found to have an elevated plasma P/TC ratio and, hence, were literally preeclamptic. The test is at present being used as a means of separating the preeclamptic group into true preeclampsia and non-convulsive cases.

A possible relationship between the elevated ratio and water balance in connection with the etiology of eclampsia has been given.

The method of estimating the plasma P/TC ratio has been outlined and the clinical value of the same briefly indicated.

NOTE: The author wishes to express his appreciation of cooperation given by various members of the staff of the Department of Obstetrics and Gynecology of the Strong Memorial Hospital, Rochester, New York.

The major portion of this work was done at Rochester, New York. Two cases were added to the list from the Nicol Wing of the Kingston General Hospital, Kingston, Ontario, Canada.

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TRIBROMETHYNOL PREMEDICATION IN OPERATIVE GYNECOLOGY

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THE gynecologist, as well as the general surgeon, now has at his disposal an extensive array of agents which can be used in the preparation of his patients for operation. For many years the usual preparation of gynecologic patients, other than local, has been the administration of a hypodermic of morphine and atropine. Twenty years ago or more, scopolamine was added in certain instances to develop the state of amnesia which was desirable in operating in certain cases. This did not lend itself to use in gynecology and hence did not become popular. During the same period there was a gradual tendency to get away from the use of deep anesthesia with ether, and nitrous oxide and ethylene with or without local infiltration were utilized.

In the past decade a refinement in preparation has appeared in that various premedications have become available, especially the numerous barbiturates. Dial, pentobarbital sodium, phenobarbital, and sodium amytal are most commonly used. Some of these may be given intra-

venously and rectally, as well as orally, and are at times valuable. In our opinion, however, they are most efficacious when administered after operation.

The first mention of tribromethynol (avertin) was by Eichholtz¹ in 1924 as a rectal anesthetic. It is tribromethylalcohol, and its chemical formula is $\text{CBr}_3 \cdot \text{CH}_2\text{OH} - \text{HBr} \rightarrow \text{CBr}_2 = \text{CHOH} \rightarrow \text{CBr}_2\text{HCHO}$.

Dosage tables have been formulated showing the amount of avertin fluid and properly warmed distilled water required for a 2.5 per cent solution. It is important that distilled water be used to prevent unfavorable chemical reactions.

It is not the purpose of this paper to discuss the technic of the administration of this product; we merely state that it is given as a rectal instillation approximately one-half hour before the patient is taken to the operating room. An enema is given the night before, but none at the time of administration. It is customary to give morphine $\frac{1}{6}$ gr. with or without atropine just before the patient is taken to the operating room.

DOSAGE

In the early days of the use of avertin it was recommended for actual surgical anesthesia. This was accomplished by giving large doses, even as much as 120 or 140 mg. per kilogram of body weight. Experience has taught that it has no place in this field but should be employed purely as a method of premedication to be followed by the use of local or, more commonly, general anesthesia. The amount used within safe limits, in our estimation, is between 60 and 80 mg. per kilogram of body weight.

VARIATIONS IN DOSAGE

A healthy young woman of average weight will take 70 mg. per kilogram, sometimes more. However, the weak, emaciated, dehydrated, or excessively obese patient should not be given more than a 50 or 60 mg. dose.

Tribromethynol is absolutely contraindicated in the presence of severe organic disease of the liver, severe bilateral disease of the kidneys, acidosis, and starvation.

ADVANTAGES

The patient usually goes to sleep with little or no excitation and frequently continues to sleep lightly after the operation for several hours; it seems to dull her pain sense much longer than ether or nitrous oxide with the result that her reactions are slower in returning. Many patients never know they were operated upon until many hours later, and all apprehension disappears.

Observers have noted that there is not as much postoperative nausea as when other agents are used; it was found that, if no ether is given,

nausea and vomiting is a postoperative complication in no more than 25 per cent of the cases (White²).

There is frequently a state of amnesia, even though the narcosis has been very light, so that the patient has no recollection of anything that happened from the time the drug was administered, even though she was never deeply asleep. In some instances this may carry over for a period of a day or more from the actual time of the operation.

The respirations are quiet, and the drug can be given safely in the presence of cardiac and pulmonary complications. Furthermore, postoperative gas pains are diminished because less ether is required. Since there is very little perspiration during the operation, there is a conservation of body heat.

PHARMACOLOGY

Many pharmacologic experiments have been made showing the effects of avertin upon various organs of the body. It is known to be excreted almost entirely through the kidneys although a small amount may pass off through the lungs. Experiments³ have shown that repeated administration of avertin in very large doses produces a mild parenchymatous degeneration of the liver and kidneys. Shipley and Karns⁴ proved it has no irritating effect upon the wall of the bowel. Field and Pilcher⁵ observed that there was usually a decrease in the urinary output during the first two or three days postoperative but not more marked than in controlled cases with similar operations.

COMPLICATIONS

The most startling complication encountered is the lowering of the blood pressure. This may be of serious moment and is the chief reason why avertin is not popular in obstetrics. Furthermore, the drop is exceptionally great in hypertension and the drug should be given very carefully in such cases.

The other complication besides the blood pressure fall which is to be feared is the effect on the respiratory center. The respirations may become extremely shallow, and, if too much opiate has been used, artificial respiration has sometimes been required.

Only last year Barlow⁶ advocated the use of sodium pentobarbital for preanesthetic medication, stating that in a series of 1,831 unselected cases from the Lakeside Hospital there was a 30 per cent incidence of postoperative albuminuria in patients receiving avertin, and found a 10 per cent incidence of shock reactions during or after the operation. This has not been borne out in our cases, unless one called every temporary drop of blood pressure a definite evidence of shock, i.e., we have not made the same interpretation of the findings.

A study was undertaken to determine the results in the use of avertin as a premedication or basal anesthetic. We concluded that its use prior

to 1930 was not of sufficient volume to be included. Therefore, all gynecologic patients operated upon by the visiting and associate gynecologic and surgical staffs during 1930, 1931, 1932, 1933, and 1934 were investigated to see if there were evidences of any advantages not found in patients operated upon without its use.

TABLE I. SUMMARY OF OPERATIONS

		NO.	NAUSEA	VOMITING	NEITHER	PER CENT
<i>Major Operations</i>						
Avertin	90 mg.	163	59	32	104	64
Avertin	80 mg.	115	52	32	71	61
Avertin	70 mg.	118	59	34	59	50
Avertin	60 mg.	47	20	14	27	57
Avertin + sodium amytal		22	8	5	14	64
Total		465	198	117	275	59.5
<i>Minor Operations</i>						
Avertin + N ₂ O-Oxygen		69	26	12	43	62
Avertin + N ₂ O-Oxygen-Ether		30	14	9	16	53
Total		99	40	21	59	58
Total Number of Cases						564

TABLE II. TIME CONSUMED IN 429 MAJOR OPERATIONS

	60" OR LESS	60-80"	80-100"	100-120"	120"+
Panhysterectomies	2	12	49	27	55
Supervaginal hysterectomies	2	17	37	16	58
Other Laparotomies	7	18	54	31	44
Total	11	47	140	74	157

NOTE:—Hysterectomies almost invariably included perineorrhaphy and incidental appendectomy. Other pelvic laparotomies included routine curettage, cauterization of the cervix, or plastic. Incidental appendectomy, together with operations for ectopic pregnancy, salpingitis, ovarian pathology, and retroversion of the uterus.

The three types of operations were almost equally divided in this series.

In 30 minor operations in which avertin was used plus gas-oxygen-ether anesthetic, 16 patients, or 53 per cent, had neither nausea nor vomiting after the operation. Nine, or 30 per cent, vomited.

In 69 minor operations in which avertin was used (always in moderate doses) *without* ether, 43 patients, or 62 per cent, had neither nausea nor vomiting, and only 12, or 17 per cent, actually vomited.

SODIUM AMYTAL

We were interested to see the effect of sodium amytal combined with small doses of avertin, and we have used it in 22 gynecologic operations, which were just reviewed. Only 5 of these patients vomited, i.e., 17, or 77 per cent, did not. However, it is important to know if the patient has any idiosyncrasy to sodium amytal, consequently 3 gr. are given the night before the operation, and, if there are no untoward results, 6 gr. are given in the morning one-half hour before the avertin.

This insures the patient's being completely asleep when she leaves her room, a fact which has frequently been commented upon with

enthusiasm by the patient. No morphine is given in these cases before operation, and only with extreme caution immediately afterwards.

We have used this combination very beneficially in the cases of 30 cesarean sections, in which the use of morphine preoperatively was not thought advisable. In such cases a weight 15 or 20 pounds less than the real weight was used in computing the dosage, to compensate for the weight of the baby, amniotic fluid, and placenta.

On one occasion morphine gr. $\frac{1}{6}$ and atropine gr. $\frac{1}{150}$ were inadvertently given after the sodium amytal and avertin, and this patient was so deeply anesthetized that a complete perineal repair and hemorrhoidectomy were performed before the patient needed any inhalation anesthetic for the laparotomy.

MORTALITY

Four patients, in 564 cases, died while in the hospital:

1. With tuberculous meningitis, three days postoperative
2. General peritonitis, fourteen days postoperative
3. Cardiac death, two days postoperative

4. An obese negress who died in 1931 had a 90 mg. dose of avertin per kilogram, was in a state of shock on the operating table, and never recovered from it. Diagnosis: Intraligamentous fibroid. Operation: Supravaginal hysterectomy; she died three hours postoperative, without regaining consciousness. Autopsy was refused. This may have been death from the anesthetic.

SEVERE IMMEDIATE COMPLICATIONS

In 1930 there were 18; in 1931, only 3; in 1932 and 1933, only 2; and in 1934, only 1.

The severe immediate complications, that of rapid and dangerous drop of blood pressure, with other evidences of shock, are in direct proportion to the dosage of avertin used. Needless to say, some patients were not in as good condition for any operative procedure as they might have been; but when the dosage is considered, the symptoms are readily explained. In 1930 a dose of 90 to 100 or more milligrams of avertin was not uncommon, and symptoms of shock were of frequent occurrence, either during the operation, or immediately after.

The picture is that of profound shock with marked drop in blood pressure: the respirations become very shallow or cease; the pulse, weak and thready; color, pale or slightly cyanotic; and the skin, clammy. It has been proved experimentally that there is not only splanchnic dilatation but also engorgement and dilatation of the coronary arteries. As a cardiac depressor, however, it is said to be only one-sixteenth as toxic as chloroform (Parsons⁷).

Treatment includes shock position, application of heat, caffeine and ephedrin hypodermically, intravenous saline or glucose, inhalation of

carbon dioxide, 4 to 10 per cent, alpha lobeline to stimulate the respiratory center, and artificial respiration.

Now to return to observations of this particular group of cases, it was noted that headache occasionally occurs the day of the operation but quickly disappears.

Pulmonary complications have been conspicuously absent, but this bears out the observation of others in this respect. The one woman who died had atelectasis, though hers was a cardiac death, proved at autopsy; there were no cases of postoperative pneumonia in the entire series. This may be ascribed to the fact that the amount of ether required is a great deal less than in those not receiving this premedication.

For a time it was thought that pentobarbital sodium would give the same desirable preanesthetic assistance, and indeed it does in some instances, without any fear of inducing shock. However, barbiturates often bring on severe excitability, which is not desirable during the several hours immediately following any operation.

NAUSEA AND VOMITING

Nausea and vomiting during the first twenty-four hours after any gynecologic operation is not desirable. With ether anesthesia it is the rule, rather than the exception, so that one frequently sees postoperative orders which say, "Give water when nausea ceases," or words to that effect. It is a safe assumption that not more than 10 per cent of all patients given an ether anesthetic escape severe nausea or vomiting.

This percentage is increased if nitrous-oxide-oxygen anesthesia is used with only small amounts of ether, but we have never seen any inhalation anesthetic that could be given with less nausea than following avertin premedication.

SUMMARY

We have made a critical study of 429 major gynecologic operations, noting the time consumed. Most of these cases included at least a perineorrhaphy in addition to the operation noted.

The time of actual operation was over two hours in 157, or 36 per cent, of these.

The absence of nausea or vomiting within twenty-four hours of operation as an evidence of good anesthesia has been reviewed in 465 cases, which showed that 198 patients were nauseated; the remainder, or 59.5 per cent, had neither. Only 117 actually vomited, leaving 348, or 75 per cent, who did not.

Among the 99 minor procedures, 59, or 58 per cent, had neither nausea nor vomiting, and 78, or 79 per cent, had no vomiting.

Giving sodium amytal with avertin has a marked hypnotic effect, and the patient is more certain to be asleep when she leaves her room, but it does not appear to influence the postoperative comfort.

The dose of avertin has gradually been diminished so that now only 60 or 70 mg. per kilogram of body weight is used. This is especially important in the obese patient or in one with hypertension.

Avertin should not be used if deep relaxation is required because it is impossible to obtain this on account of diminution of the respiratory volume. Serious complications have practically disappeared since the dose of avertin has been reduced.

CONCLUSIONS

1. Avertin is safe as a basal anesthetic in gynecology if the known contraindications and dangers are heeded.

2. It should be given by a trained anesthetist, experienced in the administration of rectal anesthesia.

3. The dose that is safe is usually not more than 70 mg. per kilogram of body weight. Serious complications attend administration of large doses, though postoperative nausea is greatly reduced.

4. Avertin can be combined with a barbiturate if it is known that there is no idiosyncrasy on the part of the patient. This insures a light sleep before leaving the patient's room, which is of marked advantage in the care of many excitable women.

5. Within twenty-four hours postoperative nausea has been found to be absent in 59 per cent of these patients, and no vomiting occurred in 75 per cent.

6. Postoperative nausea and vomiting have been found to be in direct proportion to the concentration of ether used in the inhalation anesthetic.

NOTE.—I wish to thank Mrs. Gertrude Fife and Miss Mary Lucile Goodman, of the School of Anesthesia at Lakeside Hospital, for their aid and cooperation in procuring the data which have been presented.

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10515 CARNEGIE AVE.

Ohga, T., and Aoji, Sh.: *Trichomonas Vaginalis Among Japanese Women*, Jap. J. Obst. & Gynec. 17: 364, 1934.

The authors examined 1,000 women for trichomonas vaginalis and found these organisms in 124. The incidence during pregnancy was almost the same as among nonpregnant women. Relatively few women suffer any discomfort, and only 36 out of the 124 women had any subjective symptoms. The authors failed to find any increase in puerperal morbidity among women who had trichomonas vaginalis during pregnancy.

J. P. GREENHILL.

AN EXPERIMENTAL STUDY OF THE EFFECTS OF INTRA-
VENOUS INJECTIONS OF HYPERTONIC GLUCOSE
SOLUTION (50 PER CENT) ON THE CIRCULATION OF THE CAT

II. EFFECTS OF INJECTION OF 50 PER CENT GLUCOSE SOLUTION BEFORE
AND AFTER ARTIFICIAL REDUCTION OF BLOOD PRESSURE BY TRAUMA*

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EXPERIMENTALLY,¹ we have found that 50 per cent glucose injected into the circulation of the cat will raise blood pressure and pulse pressure and will diminish pulse rate, and that preliminary injection of glucose makes experimental reduction of blood pressure by hemorrhage more difficult. Cannon and Bayliss,² in their studies on traumatic shock, demonstrated that trauma to one of the extremities of the experimental animal produces general phenomena that are closely similar to those seen in patients in shock. It has advantages over other methods of producing a fall in blood pressure in that the opposite extremity can be used as a control, and in the fact that the inflow and outflow of blood from the part can be controlled as desired. It is, therefore, the purpose of this paper to report the effects of injection of 50 per cent glucose into the circulation of cats, both before and after the experimental reduction of blood pressure by trauma.

METHODS

Cats were used in all experiments. Sodium amytal (0.1 to 0.2 gm.) injected intraperitoneally was employed as the anesthetic. The animals were anesthetized sufficiently with this amount to permit no evidence of pain when the posterior extremity was traumatized. Mean blood pressure readings were determined by placing a cannula in the carotid artery which was connected to a mercury manometer. A needle was placed in the femoral vein and connected with a buret carrying the solutions. At times the buret was replaced by an ordinary Luer syringe when rapid injections were desired.

The amount of glucose used was 6 c.c. of a 50 per cent solution (2 c.c. per kilogram of body weight). Both the slow and rapid methods of injection were used. The rapid injections were made with a Luer syringe, delivering a maximum of 8.5 c.c. per minute. In the slow method, the buret was used and the cock was set so that it delivered approximately 1 c.c. per minute.

*Read by invitation at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, November 22, 1932, and later revised to include work done in 1932 but published in 1933.

Experimental trauma was obtained by applying a tourniquet to the posterior leg, high up in the groin, and crushing the tissues below with a heavy pair of mechanics pliers. Care was taken that the bone was not broken and the skin not torn. The length of time of traumatization was ten minutes; this was always done by the same person. The tourniquet was released within five to ten minutes following the trauma and the experiment continued. This method of producing shock is almost identical with the method described by Cannon and Bayliss.²

EXPERIMENTAL RESULTS

The effects of the intravenous injection of 6 c.c. 50 per cent glucose into the circulation of cats, with an artificial reduction of blood pressure by injury to the leg, were determined in twenty experiments. Two groups are presented: one in which no glucose was given before trauma, and the other in which 6 c.c. of 50 per cent glucose were injected before trauma. Both groups received glucose following the leg injury.

CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA (INJURY TO LEFT LEG)

Group I. Without Previous Glucose (10 cats).

1. *Blood Pressure:* Following trauma the blood pressure fell an average of 20.7 mm. Hg. When glucose was administered (6 c.c. of 50 per cent), the pressure began to rise, reaching a high level average of 98 mm. Hg, or 7.33 mm. above the original. Hence, following glucose the pressure rose so that the fall was obliterated, and the sustained level was slightly above normal (average normal 82.66. Hg average sustained level after glucose injection, 84.66 mm. Hg, see Tables I, II, and III).

TABLE I. TEN CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA FOLLOWED BY INJECTION OF GLUCOSE

	ORIGINAL	TRAUMA	6 C.C. 50% GLUCOSE
Blood pressure (mm. Hg)	82.66	61.33	84.66
Pulse pressure (mm. Hg)	3.66	3.75	5.41
Pulse rate (per min.)	143.0	138.3	128.0

TABLE II. TEN CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA WITH GLUCOSE BEFORE AND AFTER TRAUMA

	ORIGINAL	6 C.C. 50% GLUCOSE	TRAUMA	6 C.C. 50% GLUCOSE
Blood pressure (mm. Hg)	87.3	104.30	91.3	106.60
Pulse pressure (mm. Hg)	3.66	5.66	4.33	6.33
Pulse rate (per min.)	155.0	146.60	134.0	126.60

TABLE III. TWENTY CATS WITH BLOOD PRESSURE LOWERED ARTIFICIALLY BY TRAUMA

	NO GLUCOSE BEFORE	6 C.C. 50% GLUCOSE BEFORE
	TRAUMA—INJURY LEFT LEG	
Blood pressure (mm. Hg)	-21.33	-13.0
Pulse pressure (mm. Hg)	+ 0.09	No change
Pulse rate (per min.)	- 4.70	-12.6

2. *Pulse Pressure:* The final pulse pressure was increased above the original. Trauma showed an increase of 0.66 mm. Hg. After glucose, the pulse pressure showed a further increase of 1 mm. Hg (see Tables I, II, and III).

3. *Pulse Rate:* There was a definite decrease in the pulse rate. A final average difference of 15 beats per minute (see Tables I, II, and III).

Group II. With Previous Glucose (10 cats).

1. *Blood Pressure:* The original injection of 6 c.c. 50 per cent glucose elevated the blood pressure above the original, from 87.3 mm. to 104.3 mm. Hg. Following

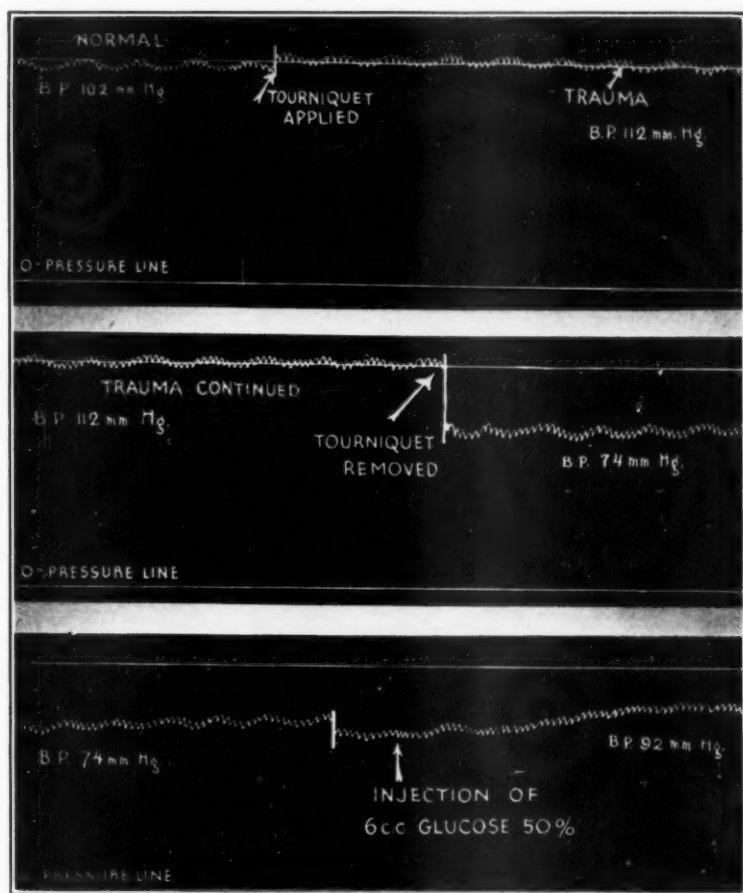


Chart 1.—Response to injection of 6 c.c. of 50 per cent glucose after trauma—injury to left leg.

trauma the blood pressure fell sharply, but the low level was only a few millimeters below the previous normal (80.6 mm. Hg). Within less than one minute the blood pressure began to rise so that the sustained pressure increased, reaching a high point of 108.0 mm. Hg. This was maintained at 106.6 mm. Hg (i.e., 19.3 mm. above the original (see Tables II and III).

2. *Pulse Pressure:* The pulse pressure was increased as a rule. In one case it returned to normal (see Tables II and III).

3. *Pulse Rate:* The pulse rate in all cases was slowed an average of 29 beats per minute (see Tables II and III).

DISCUSSION

Injection of 50 per cent glucose into cats, with a blood pressure artificially reduced by trauma, produced a characteristic reaction in all cases. There was always a rise in blood pressure, an increase or a return to the original pulse pressure, and a slowing or a return to the

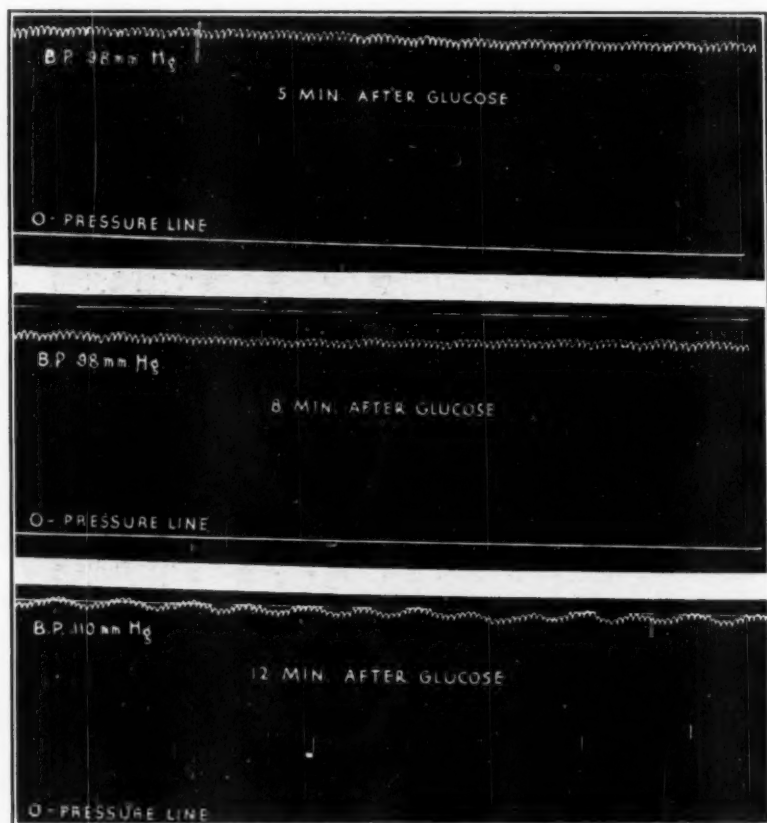


Chart 2.—Continued response to injection of 6 c.c. 50 per cent glucose after trauma—
injury to left leg.

original pulse rate. The initial degree of fall in blood pressure upon the release of the tourniquet following trauma was about the same whether glucose had been given previously or not. But in cats in which a fortifying dose had been given, there was the tendency for the blood pressure to rise again subsequent to the trauma. The sustained fall in blood pressure in this series was less than the fall in the animals without the previous injection of glucose. Hence, the final maintained blood pressure level was much higher after trauma when glucose had been previously

given. These findings would indicate that a fortifying dose of glucose resists the fall in blood pressure following artificial reduction of blood pressure by trauma.

Following the administration of glucose after trauma the blood pressure was increased as a rule. The pulse pressure was closer to the

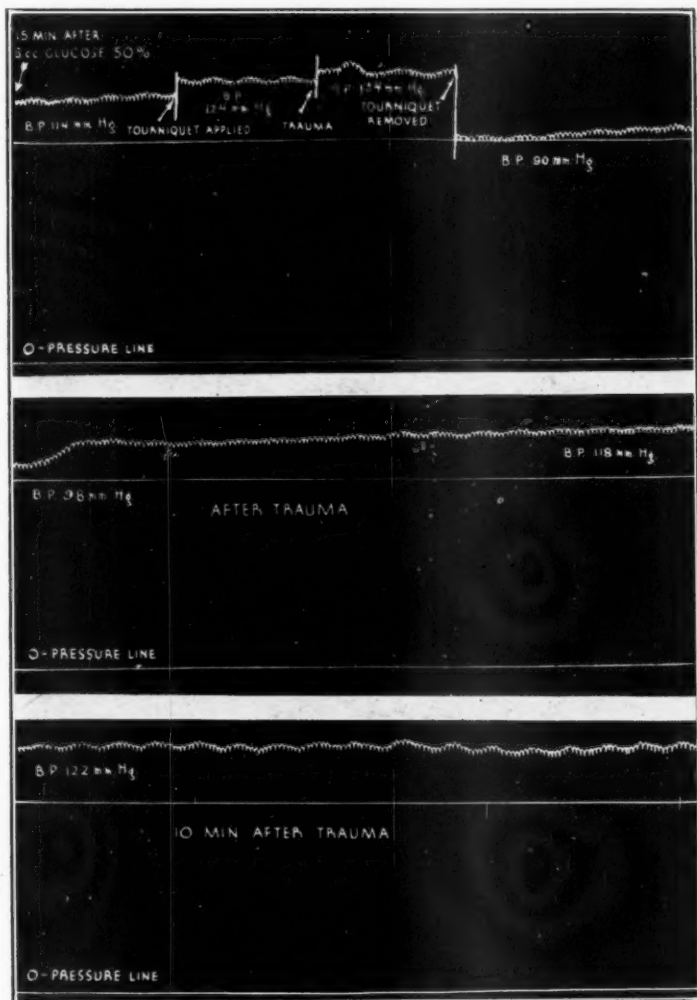


Chart 3.—Response to trauma fifteen minutes after injection of 6 c.c. of 50 per cent glucose.

original in the series of animals that had received previous glucose than in those cases in which no initial glucose was given. The pulse rate in all cases was slowed after glucose injection.

Tables I, II, and III present the significant average findings. Charts 1, 2, 3, and 4 are characteristic tracings taken from both groups.

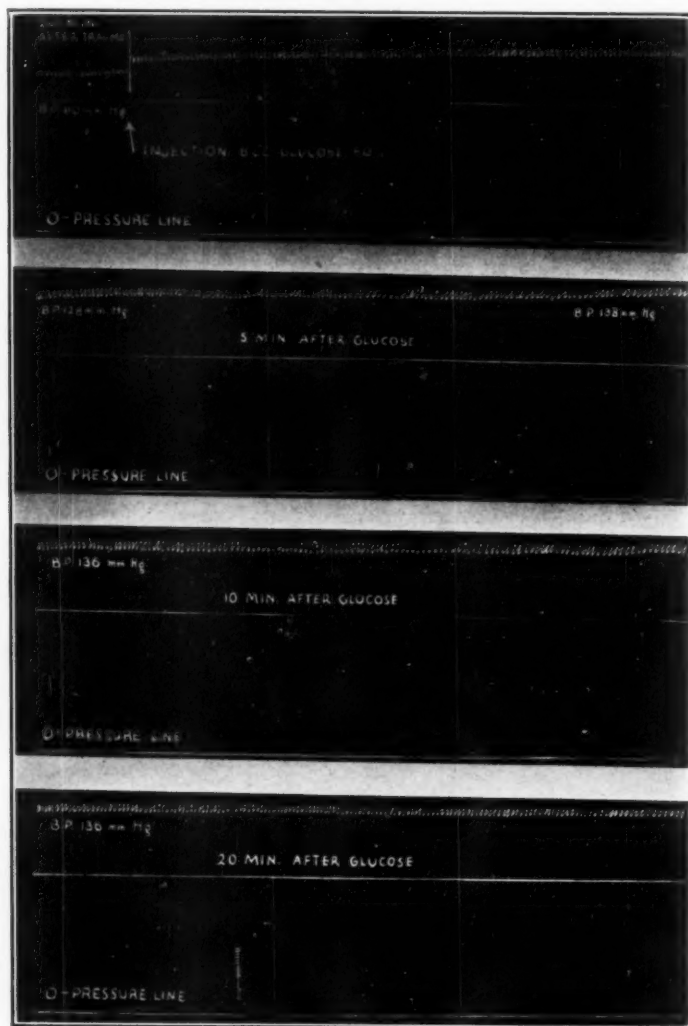


Chart 4.—Response to second injection of 6 c.c. of 50 per cent glucose twenty minutes after trauma with previous administration of glucose.

SUMMARY AND CONCLUSIONS

In experiments on cats anesthetized by intraperitoneal sodium amytal, the effects of the intravenous injection of 50 per cent glucose before and following trauma to one of the extremities were studied. As a result of our findings we conclude that:

1. Fifty per cent glucose injected intravenously into cats with a blood pressure artificially reduced by trauma produces a sustained rise in blood pressure.
2. It causes a sustained rise in pulse pressure.

3. It produces a sustained diminution in pulse rate.
4. Preoperative injection of 50 per cent glucose diminishes the fall in blood pressure due to trauma.

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133 CLINTON STREET

BLASTOMYCOSIS OF THE FEMALE REPRODUCTIVE TRACT*

WITH REPORT OF A CASE

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GENERALIZED blastomycosis (American Blastomycosis, Gilchrist's disease) can no longer be considered a clinical rarity in view of the numerous case reports in the recent literature. The fungus has been known to produce lesions in almost every organ in the body, including the male reproductive organs. Infection of the body of the uterus and of the tubes has never been described to our knowledge. This may be because blastomycosis is comparatively rare in women and not because the reproductive organs of the female have increased resistance to infection with this fungus. Less than a tenth of the reported cases of systemic blastomycosis occurred in this sex.

There is a report of primary blastomycosis of the cervix in a Paraguayan woman.¹ A biopsy of the cervix showed miliary abscesses and double contoured bodies but no giant cells or blastomycotic tubercles. The organisms could not be cultivated. Palpation indicated that the deeper pelvic organs were not involved.

No account of significant blastomycotic lesions of the vagina was found. References to fungous infections of the vagina were usually concerned with monilia,² and it was not definite that the yeasts found in cases of vaginitis had an etiologic bearing. Castellani stated³ that fungi are frequently encountered in vaginal discharges but that he never noted the fungus described by Gilchrist.

The following case is added to the literature as the first recorded case of blastomycotic infection of the endometrium, myometrium and

*Submitted for publication June 4, 1935.

tube. It is of further interest in that the diagnosis was established by examination of the curettings before laparotomy.

Clinical Report.—Mrs. V. S., aged twenty-seven years, white, para 3-0-3, was first seen by the gynecologist on Apr. 2, 1935, when she was referred by the orthopedist because of irregular, too frequent and profuse menses (polyhypermenorrhea). She had been under observation and treatment by the medical and orthopedic services since July, 1934, because of blastomycosis of the lungs and a compression fracture of the twelfth dorsal vertebra. Menstrual irregularities were first noted upon the return of menses following the birth of her last child, Nov. 27, 1933, when menses began to occur approximately every three weeks with increase in the duration of the flow from four to seven days and a proportional increase in the amount of blood loss as judged by napkin count and pad saturation. During the past several months prior to admission, the menses had been very irregular and excessive. The last menstrual period began fifteen days prior to admission and still persisted at the time patient was first seen. The period previous to this had occurred seven days before and lasted only one day. Two weeks before this, there had been an excessive period of seven days' duration. There had been no unusual symptoms associated with these irregular menses except evident weakness due to excessive blood loss. The patient complained also of abdominal symptoms which had become more pronounced in the last six to eight months. Low grade lower abdominal pain and tenderness increased. The patient had noticed some "swelling of the abdomen" and "bulging" when she was upright. Constipation had become more severe during this time. There had been no obstructive symptoms; appetite had been good.

Family history was unimportant. Past health had been good until the past year. An attack of "kidney colic" occurred in March, 1934; three cystoscopic treatments were received. A hemorrhoidectomy was performed in April, 1934. Her back was injured by a fall in April, 1934. Pain in the chest and a productive cough of three months' duration caused the patient to be seen in Duke Hospital for the first time, July 8, 1934. A diagnosis of pulmonary blastomycosis was made from pus obtained by bronchoscopic examination. Treatment with iodides, vaccines, and x-ray resulted in satisfactory arrest of the pulmonary condition. A fracture of the twelfth dorsal vertebra resulting in progressive weakness of the lower extremities was discovered at this admission. This was treated with splints and braces by the orthopedists. A definite diagnosis of blastomycosis of the spine was not made. The patient was discharged from the hospital Oct. 23, 1934. There had been four subsequent admissions to Duke Hospital (Dec. 3-6, 1934; Jan. 22-24, 1935; Feb. 4-6, 1935; Apr. 1-25, 1935, present admission) for observation and treatment of her pulmonary and spinal condition during which time progressive improvement had been reported.

Marital history included three normal pregnancies, labors, and puerperia, all children being alive and well; the youngest child was born Nov. 27, 1933. The patient lived in a small hamlet in North Carolina; cared for own household; had not been overworked; and was of temperate habits.

Physical Examination.—The patient was well nourished and well developed, and was in no acute distress. Her weight was 136 pounds. General physical examination was essentially negative except for evidences of the fractured vertebra and the pelvic findings. No abnormal signs were elicited on chest examination, and the x-ray examination showed the old lesion in the upper left lobe well healed. The orthopedic condition showed improvement; there was slight weakness of the lower extremities; however, the patient was able to walk with the use of the braces with which she had been supplied. Pelvic examination showed a moderate relaxation of the perineal floor with moderately atonic levator muscles, with a slight rectocele and slight sagging of the bladder base. The external genitals were normal otherwise.

Bartholin's and Skene's glands and urethra were normal. The cervix was of normal consistency, directed slightly upward, movable with moderate pain. Speculum examination showed a slight chronic endocervicitis of the ulcerative type. There was moderate old serosanguineous vaginal discharge. The uterus was in midposition, slightly softened, of approximately normal size, moderately fixed, and movable with moderate pain. There were two masses about 3 to 3½ inches in diameter, quite tender and relatively firm, one upon each of the lateral surfaces of the uterus. The mass on the right side was more lateral and was situated in about the midportion of the pelvis. The mass on the left side, which was slightly larger than the one on the right side, was associated with the posterior and lower surface of the uterus and seemed to be rather firmly fixed to the culdesac. Neither of these masses could be separated completely from the uterus. Tubes and ovaries could not be outlined as such. No other pelvic masses could be felt. A preliminary diagnosis was menorrhagia and metrorrhagia (probably of inflammatory origin, chronic endometritis) and bilateral tuboovarian masses. A blastomycotic infection of the pelvic organs was considered in view of the patient's previous record. The possibility of peritonitis from the same organisms was suspected because of the abdominal symptoms. A diagnostic curettage was advised in order to establish the etiology of the bleeding.

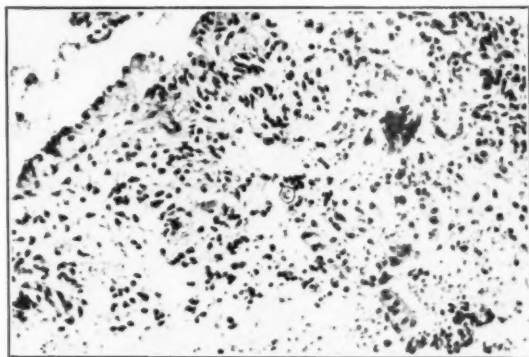


Fig. 1.—Fragment of curettage from uterine cavity showing endometrial blastomycosis. An organism with double contour lies in the center of the figure. Upward and to the right is a giant cell. The stroma shows subacute and chronic endometritis. Upward and to the left is endometrial epithelium. $\times 200$.

Laboratory Findings.—Hemoglobin 72 per cent (Sahli); R.B.C., 3,720,000; W.B.C., 16,050; differential: polymorphonuclear leucocytes 83 per cent, large mononuclear leucocytes 2 per cent, small mononuclear leucocytes 12 per cent, transitionals 0 per cent, eosinophiles 2 per cent, basophiles 1 per cent; blood cells of normal morphology. Urinalysis: (noncatheterized) yellow, clear, 1,009, acid, no sugar, no albumin, no acetone, 5-7 white blood cells, no red blood cells, no casts. Sedimentation time 6 mm. in first 30 minutes.

Operative Findings and Treatment.—On Apr. 4, 1935, examination under N_2O and O_2 anesthesia revealed no additional abnormalities. Dilatation and curettage yielded a moderate amount of endometrium from which diagnosis of blastomycosis of the endometrium and endocervix was made by one of us (see pathologic report). Blastomycetes were cultured from swabs taken from the uterine cavity at the time of curettage (see bacteriologic report).

Possible methods of treatment were discussed after determining the infecting agent. It was decided to perform a laparotomy with removal of the uterus and tuboovarian masses. In arriving at this decision we consulted with members of our own department and with Dr. D. T. Smith. We felt that little benefit could be expected

from curettement alone in the presence of the bilateral tuboovarian masses. We believed that radiation of the pelvic viscera in the presence of such evident infection was not justified and that the results of such radiation of the active ovarian tissue would be more harmful than surgical ablation. It was felt that, if the infection were localized to the pelvis and if all of the involved tissue could be removed, the ultimate prognosis might be good; however, if there were extensive abdominal and peritoneal involvement, as the history suggested, the removal of the pelvic focus would be beneficial although the prognosis would still be grave. The possibility of poor healing of the abdominal wound with fistulas had to be considered. Dr. Smith thought the patient could tolerate surgical anesthesia and that no anxiety should be felt because of possible trouble from her previous pulmonary lesions.

Laparotomy was performed on Apr. 8, 1935, following routine preoperative preparation. Anesthesia was induced with nitrous oxide and oxygen and then was changed to drop ether. The abdomen was opened through the usual midline incision. Approximately four quarts of clear straw-colored fluid were aspirated from the peritoneal cavity. Inspection showed a diffuse involvement of the pelvic parietal peritoneum with multiple small grayish miliary tubercle-like nodules about 1 mm. in diameter. The omentum which had come well down into the pelvis and was adherent to the matted pelvic viscera was studded with similar nodules. The sigmoid was adherent to the left side of the pelvic mass and several loops of small intestine were bound by dense adhesions to the upper portion of the mass. These, as well as other loops of intestine in the lower abdomen, showed studding similar to that appearing on the peritoneum. The anterior surface of the uterus was firmly adherent to the vesical peritoneum. In several areas of the broad ligaments the nodules coalesced and appeared as grayish plaques. The intestinal and omental adhesions were freed carefully by sharp dissection, ligated, and cut so that finally the pelvic masses could be outlined. The uterus, which was adherent in its anterior and upper surface to the bladder and the bladder peritoneum, was of normal size and in anterior position. The right tube was red, thick, tortuous, about 1 inch in thickness, and arched acutely down into the culdesac, where it was densely adherent to a right tuboovarian mass about 3 inches in diameter. This mass was densely adherent to the undersurface of the right broad ligament which was about $\frac{3}{4}$ inch thick, and to the lower right border of the uterus and to a loop of small intestine (Fig. 2). The mass was freed carefully by blunt and blind dissection and in the process of delivery ruptured, expelling about 10 c.c. of creamy, thick yellow pus which were aspirated and reserved for bacteriologic examination. The tuboovarian mass was freed from its broad ligament and uterine attachments and removed. The left tube, thickened and tortuous, was not as enlarged or as indurated as the right one. It measured approximately $\frac{1}{2}$ inch in its greatest diameter. It was also intimately associated with a tuboovarian mass about $3\frac{1}{2}$ inches in diameter which lay beneath the left broad ligament and was adherent to the culdesac. The mass was partially covered anteriorly by the sigmoid to which it was adherent. The mass was freed by blunt dissection and, in the process of delivery, ruptured. About 15 c.c. of thick creamy pus were aspirated and were saved for examination. The tuboovarian mass was excised. Supravaginal hysterectomy and routine pelvic repair were done. A Penrose drain was inserted well down into the culdesac and brought out through the left low abdominal stab wound. The appendix was left untouched. The abdomen was closed in the usual manner, and the usual dressings applied.

The patient stood the operative procedure and anesthesia well. Her pulse was 92 at the conclusion of the operation.

Postoperative care, in addition to the usual measures, included placing patient in moderate Fowler's position as soon as she reacted sufficiently, withholding fluids and nourishment by mouth for five days, and supplying saline by hypodermoclysis.

Postoperative convalescence was good except for a rapid pulse rate, as high as 140, which gradually became normal by the fifth postoperative day. Highest postoperative temperature was 38.6° C., reached on the second day. Temperature was normal on the sixth day. There was no rise in the leucocyte count. Distention was not marked. Skin clips and drain were removed on the fifth day. Wound showed healing by first intention, and site of drainage filled in rapidly. Wound was dressed

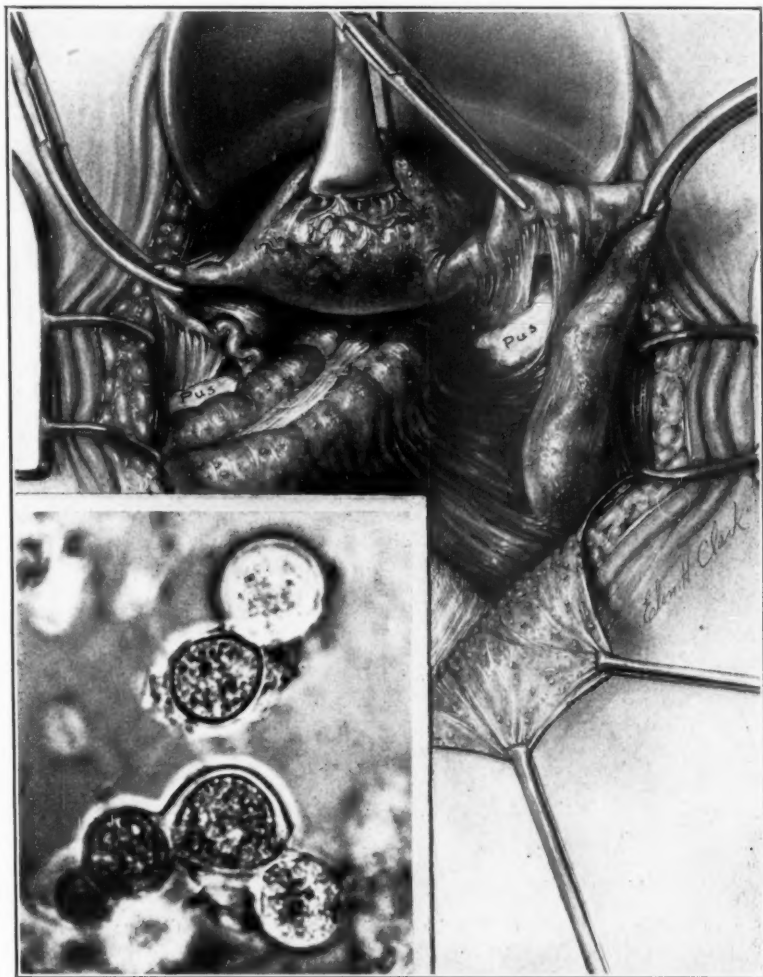


Fig. 2.—Appearance of pelvis and lower abdomen at laparotomy. The enlarged right tube, the bilateral pelvic abscesses, and the studding of the peritoneum with the blastomycotic tubercles are shown. Insert shows a fresh smear preparation of pus from the pelvic abscesses stained with tincture of iodine.

frequently and painted with 1 per cent aqueous solution of gentian violet. On the eleventh day all the silkworm-gut sutures were removed; a small stitch abscess was found about one silkworm-gut suture; culture of this showed no blastomycetes but hemolytic *staphylococcus aureus*. The patient complained of a catching pain in the left lower chest on the fifteenth day. Dr. Smith could find no abnormal chest signs, and an x-ray picture of the chest showed no recent change. The patient was dis-

charged from the hospital Apr. 25, 1935. The abdominal wound was well healed, and the pelvic condition was satisfactory except for moderate induration in both adnexal regions. She was to continue the use of braces, to continue potassium iodide, and she was referred to her local physician for further dressings and observation. In reports from patient, May 25, 1935, no untoward symptoms were described.

Comments on Clinical Course.—One is led to suspect from the duration of menstrual symptoms that the pelvic involvement occurred early in the course of the disease. This is in accord with the pathologic findings (q. v.).

The choice of surgery proved to be wise as shown by the postoperative course. Poor healing and fistulas had been anticipated. Gentian violet (aqueous solution) was used in liberal quantities, especially for irrigation of the drainage site because of its inhibiting action on the growth of blastomycetes, as shown by Sanderson and Smith.⁴

It is possible that the earlier treatment of this patient with a combination of vaccines and potassium iodide played an important rôle in making her a good sub-

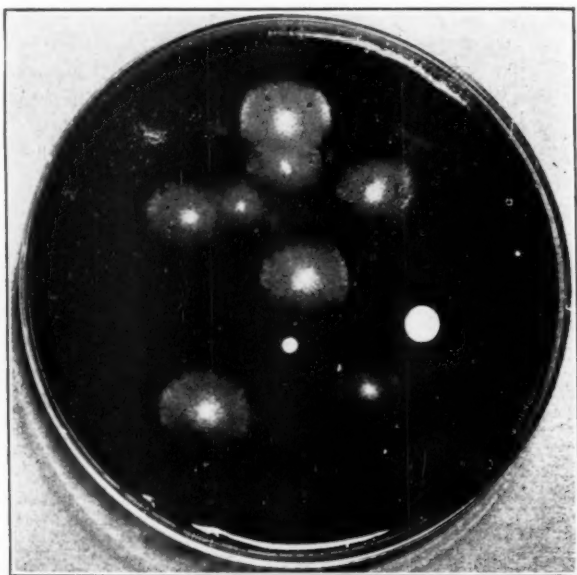


FIG. 3.—Blood agar plate inoculated by mincing a small portion of the uterus with scissors and streaking heavily over the plate. Two colonies of *Staphylococcus albus* were planted on the plate for comparison. The plate was photographed after eight days' growth at room temperature.

ject for operation. In spite of the fact that she had had the disease for more than a year, her general state of health seemed excellent.

The prognosis is, of course, guarded, but it is felt that a large residual focus was removed and that with continuation of the medical treatment, the ultimate result may be good.

The details of medical treatment will be the subject of a future communication by Smith and Martin.⁵

BACTERIOLOGIC STUDY

As noted in the case history, blastomycetes were seen in smear and cultured from the pus obtained at bronchoscopy.

At the time of curettage, swabs were planted on blood agar slants and dextrose agar slants. Eight colonies of blastomycetes appeared after eight days' incubation at room temperature.

At operation cultures were made of the peritoneal fluid, left tube, left ovary and uterus. Fresh smears all showed numerous budding, double-contoured blastomycetes (see Fig. 2 for appearance of organisms in pus from the peritoneal cavity). The solid bits of tissue were minced with sterile scissors and smeared over the surfaces of blood agar and dextrose agar plates and incubated at room temperature and at 37° C. All cultures yielded blastomycetes, but it was interesting to note that the fungus grew more rapidly on blood agar plates incubated at the lower temperature (Fig. 3).

Morphologically and culturally the fungus isolated from this patient conforms in all details to the organisms isolated from many other cases of generalized blastomycosis. The cultural characteristics have been adequately described by Stoher,⁶ Benham,⁷ and many others. Serologic studies by one of us⁸ have shown that the fungus obtained from this patient was identical with the blastomycetes of four other cases of generalized blastomycosis.

Complement fixation tests with different strains of blastomycetes were made at frequent intervals throughout the course of the disease, and all tests were strongly positive with all strains of blastomycetes tested. The complete protocols of the complement fixation tests with serum from this patient are reported elsewhere.⁸

PATHOLOGIC STUDY

The tissue from the curettage of the uterine cavity formed a mass which amounted to less than 1 c.c. in volume. The individual pieces measured 1 to 3 mm. across, and were soft and pinkish gray.

The microscopic section of the curettings, which had been embedded in paraffin, sectioned, and stained with hematoxylin and eosin, showed endometrial tissue for the most part, but fragments of endocervix were also present.

The cellular exudate in the pieces of endometrium consisted of polymorphonuclear neutrophils in large numbers, eosinophils in small numbers, and varying numbers of lymphocytes, plasma cells, and large mononuclear cells. Giant cells were noted rarely. One giant cell contained well over a hundred nuclei. In addition to the cellular reaction, there was much fibrosis, but no tubercles.

Double-contoured bodies (Fig. 1), free and also within giant cells, were seen in the endometrial stroma. Approximately a dozen bodies occurred in the whole section. The average diameter was from two to four times that of a red blood cell. The peripheral ring was hyaline and the central part either clear or provided with several granules which stained with the hematoxylin. One of the bodies, enclosed within a giant cell, had knoblike processes or buds.

The same tissue reaction was noted in some of the fragments of endocervix.

The blastomycetes were similar in all respects to the organisms observed in a case of generalized blastomycosis which had come to necropsy.

The diagnosis of blastomycosis of endometrium and endocervix was made.

The tissue received from the abdominal operation four days after the curettage of the uterine cavity consisted of the body of the uterus, the right tube, the left tube and ovary, and a piece of omentum.

The body of the uterus was little if any enlarged. It measured 5 cm. from the level of amputation to the top, 3.5 cm. anteroposteriorly, and 5.5 cm. from side to side. The serosal surface showed several red fibrous thickenings. Sagittal section of the uterus (Fig. 4) disclosed a narrow uterine cavity with a brown discoloration which extended 2 mm. into the uterine wall. Multiple parallel slices on each side of the midline showed nothing additional.

The right tube was in two pieces (Fig. 5). The longer, cone-shaped part, measuring 10.5 cm. in length and 2.5 cm. in greatest diameter, was attached to the

uterus by the narrow end and the distal end was yellow, granular, and fibrous. The other piece of right tube, which was at first thought to be the right ovary, measured 4.5 by 3 by 2.5 cm. One end corresponded to the distal end of the longer piece of tube. The serosa of both pieces was red, rough and covered with granular and taglike excrescences. Longitudinal section of both pieces showed a thickened, scarred peripheral zone and a central yellow, opaque, firm region. In the very center



Fig. 4.—Sagittal section of uterus. Curettage had been performed and accounts for some of the discoloration lining the cavity. The deeper part is due to blastomyositis. Most of the myometrium appears normal. The fibrous peritoneal thickenings are evident as darker surface elevations.

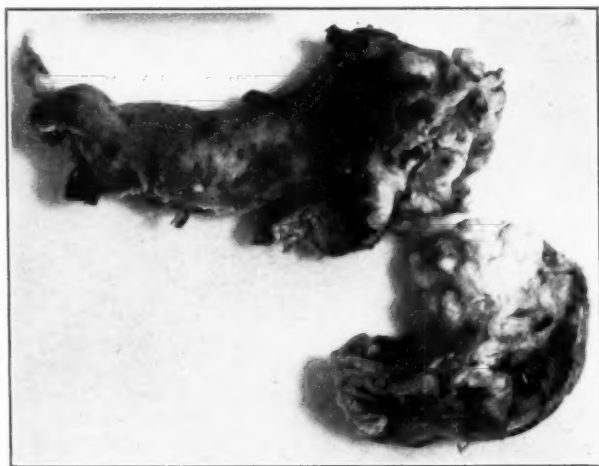


Fig. 5.—The right tube, eroded into two pieces. The narrow tapering end of the longer piece was attached to the uterus.

the tissue was friable and pus was noted, especially in the narrow end of the longer piece. The shorter piece contained a cavity 1 cm. in diameter. Sections of both pieces were made at various levels, but nothing resembling ovarian tissue was noted.

Apparently the right tube had been eroded through at a point about two-thirds of the distance from the uterus to the fimbriated end.

The fallopian tube on the left was 3.5 cm. long. The surface was rough, but the tube contained none of the yellow tissue seen in the right one.

The left ovary measured 3 by 2 by 2 cm. The surface was red and granular, but its substance was free of the blastomycotic process.

The piece of omentum had a scarred exterior.

Microscopic sections of the uterus showed that the red fibrous serosal thickenings noted grossly consisted of vascular scar tissue in which tubercles occasionally occurred. The same peritoneal reaction was noted on the surfaces of both tubes, the left ovary, and the piece of omentum.

At the fundus of the uterus, where the endometrium had not been removed by the curette, there were tubercles with central giant cells, both in the endometrial stroma and in the immediately subjacent myometrium (Fig. 6). Blastomycetes were fairly frequent in the giant cells.

Along the cavity, just above the level of amputation, the tubercles extended as much as 4 mm. into the uterine wall. They were of two types, those with central giant cells and those with centers of pus. Further out in the myometrium there was moderate perivascular lymphocytic and plasma cell infiltration, but no tubercles.

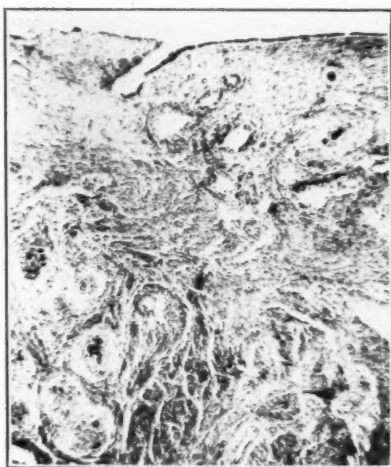


Fig. 6.

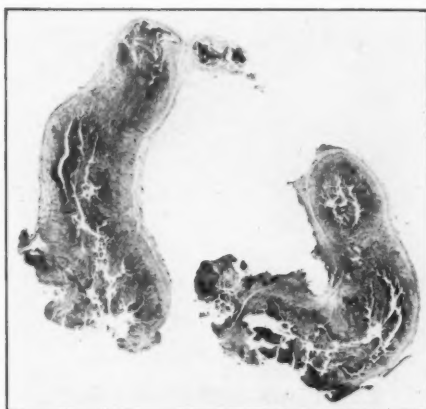


Fig. 7.

Fig. 6.—Section from the fundus of the uterus showing two blastomycotic tubercles in the endometrium (upper right) and three in the myometrium (lower left). $\times 33$.

Fig. 7.—Section of the two pieces of right tube. There is extensive fibrosis of the walls, and pus occupies the narrow, uterine end of the longer piece. $\times 1.2$.

There was no widespread active process extending in an uninterrupted fashion from the uterine cavity into the tubes since microscopic sections of the interstitial portions of each tube showed only some granulation tissue beneath the epithelium.

A large microscopic section of the two pieces of the right tube (Fig. 7) demonstrated the great fibrous thickening of the peripheral part of the tube with many polymorphonuclear neutrophils infiltrating this fibrous layer. More centrally, tubercles were numerous, and eosinophiles were present. Blastomycetes were visible under low magnification. Most of the tubercles had central giant cells as in the endometrium (Fig. 6). Others had a central area of pus and an encircling zone of fibrous tissue (Fig. 8). In several places great collections of giant cells containing blastomycetes were noted (Fig. 9). The eroded surfaces of the pieces of the tube presented small areas of necrosis, and necrotic tissue was also seen on the outside of the tube in a few places.

The longitudinal folds of the tubal mucosa were partly preserved and were swollen and infiltrated with lymphocytes and other cells. In addition, the central region

showed an interesting irregular proliferation of mucosal epithelium, undoubtedly due to attempts at regeneration. Within the tube there was almost no necrosis or caseation. The lumen was, on the other hand, filled with blastomycotic granulation tissue. The more proximal, narrow part of the tube was filled with pus (Fig. 7) consisting of polymorphonuclear neutrophils and a few macrophages and giant cells. The organisms in the pus were both free and within giant cells.

The distal part of the tube and some of the fibrous tissue adherent to the outside of the proximal portion were studied further in several microscopic sections, but no tissue resembling an ovary was located.

A section of the left tube revealed only a minimal degree of inflammatory reaction about the lumen, consisting of a few lymphocytes beneath the intact epithelium.

The section of the left ovary showed no involvement of the ovary itself, although the surface was covered with blastomycotic granulation tissue.

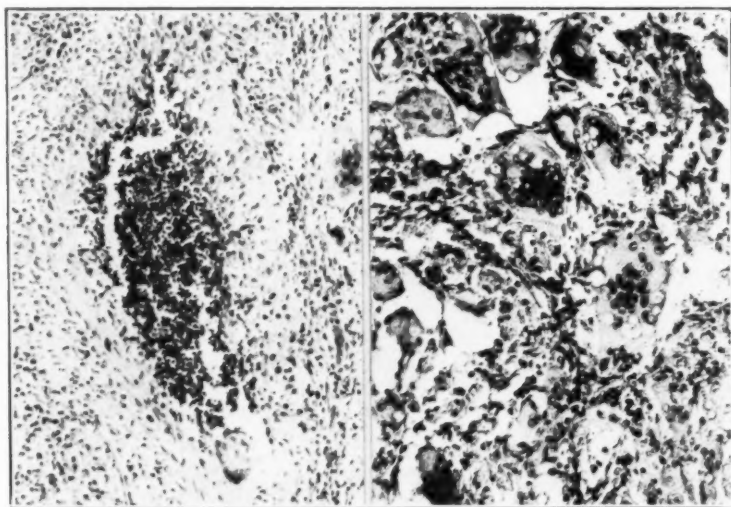


Fig. 8.

Fig. 9.

Fig. 8.—Miliary abscess in wall of tube, with surrounding fibrosis and adjacent giant cells. $\times 135$.

Fig. 9.—Giant cell reaction in wall of tube. Many of the paler bodies within the giant cells are blastomycetes. $\times 215$.

A search was made for tubercle bacilli in sections of the uterine cavity and of a part of the right tube which contained pus, giant cells, and caseation. No acid-fast organisms were noted, while a control section from a known case of tuberculosis stained simultaneously showed numerous acid-fast organisms. In addition, the counterstain of Loeffler's methylene blue failed to show any other kind of bacteria in the present case.

A diagnosis of blastomycosis of the right fallopian tube, endometrium, myometrium, and peritoneum was made.

Summarizing the pathologic findings, the lesions which have just been described could be divided into at least four forms.

First, the most prominent appearance was that of nodules or tubercles with giant cells which often contained the blastomycetes. These tubercles were especially numerous in the wall of the tube, but were also to be seen along the uterine cavity (Fig. 6) and in the peritoneum. Second in prominence were abscesses. They were chiefly

miliary abscesses with dense fibrous walls (Fig. 8). These, like the tubercles, occurred in both uterine wall and tube. Organisms could usually be found in or about them. Larger accumulations of pus, such as that free in the proximal end of the tube and those in the abscess pockets on the posterior side of the broad ligament, belonged to the same group. A much less conspicuous place was taken by a third form of tissue change, that of necrosis. This occurred at the eroded junction point of the two pieces of tube and also on the outside of the tube, probably in relation to the abscess pockets. It looked much like the caseation of tuberculosis, but it was undoubtedly due to the blastomycetes, since other organisms could not be demonstrated in or about it. The fourth type of change was that of fibrosis, which was extensively developed in the tube and on the peritoneum.

The specific forms of reaction just enumerated represented the progressive development, over a long period of time, of the exudative and proliferative response of the tissue. The conglomeration of these processes in the region of the nodules and miliary abscesses gave the appearance of blastomycotic granulation tissue, a term which might be applied as appropriately to blastomycotic lesions as the term tuberculous granulation tissue is applied to tuberculous lesions.

In brief, the tissue reactions in the operative material corresponded to what has been repeatedly described in reported cases of blastomycosis.

Gilchrist and Stokes⁹ wrote that the lesions were characterized by "the production of miliary abscesses and the formation of tubercle-like nodules."

Hektoen¹⁰ wrote as follows concerning the morphologic changes in blastomycosis:

"Study of human material as well as material from inoculated animals shows that the microorganisms in question may induce the formation of an inflammatory granulation tissue with numerous giant cells of the Langhans type associated with more or less extensive suppuration. The relative predominance of proliferative or suppurative processes appears to vary under various conditions. In loose connective tissues, such as the subcutaneous, there seems to be a distinct tendency to abscess. Microscopically, the more or less nodular lesions in which the proliferative changes are well marked present certain general resemblances to those of tuberculosis."

That the general appearance of the lesions, both grossly and microscopically, is remarkably like that of tuberculosis has been emphasized repeatedly. D'Aunoy and Beven¹¹ in reporting a series of cases of blastomycosis, stated that "only the presence of the specific organisms either active or dead, allowed making an histologic differentiation from tuberculosis in any of the cases."

This statement applies with equal force to our case.

It is interesting to speculate regarding the entrance and spread of the blastomycotic process in the body of the patient.

How did the organisms originally enter the patient's body?

The patient had apparently never had cutaneous blastomycosis from which the generalized lesions might have developed. D'Aunoy and Beven state that "usually, the occurrence of visceral blastomycotic involvement is secondary to cutaneous lesions caused by the parasites; but . . . systemic involvements need not necessarily be secondary to cutaneous manifestations, or at least can occur as sequelae to superficial lesions not sufficiently grave to cause notice thereof to be taken."

Stober put more emphasis on the respiratory tract as the portal of entry of the organisms: "In at least fourteen of the cases reported the first symptoms were referable to the lungs, and of eleven necropsies in these cases, nine presented old bronchopneumonic lesions. It is also possible that the subcutaneous abscesses or cutaneous lesions marking the onset in other patients were due to unrecognized pulmonary lesions with metastases in the skin and elsewhere."

How did the uterus and right tube become infected?

The tissue reaction in the right fallopian tube appeared older than that in the uterus since the former showed far more fibrosis. The spread seemed therefore to have been from the fallopian tube to the uterine cavity and to the peritoneum. There was probably a hematogenous dissemination from the lungs with a colonization of the organisms in the tube, from which they spread to the uterine cavity and to the peritoneum. This type of spread is analagous to what probably occurs in tuberculosis, the tissue reaction of which is much like blastomycosis. Had the organism, like the gonococcus, entered by the vagina, an infection of the cervical canal, with early symptoms from that region and an advanced process there or in the uterine cavity at the time of operation, might have been expected.

SUMMARY

Recorded cases of fungous infection by blastomycetes of the female reproductive tract were not found in the literature, with the exception of one instance of cervical blastomycosis.

A case is reported of infection of the fallopian tube and uterus with *Blastomyces dermatitidis* in a patient with arrested pulmonary blastomycosis (American type, Gilchrist's disease). A preoperative diagnosis of uterine involvement was made from a section of endometrial curettings and confirmed by culturing the organism.

Mycologic and anatomic studies of the removed tissues are recorded. These constitute apparently the first report of extensive blastomycosis of the female reproductive tract. The tissue reaction in the affected organs was remarkably like that in tuberculosis but was to be differentiated from the latter by the presence of the double-contoured blastomycetes.

The removal of the uterus was necessary to prevent further excessive blood loss, and the extirpation of the tuboovarian masses was apparently indicated to eliminate the large blastomycotic focus. The uncomplicated postoperative course seemed to have justified surgery in this case.

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AN ANALYSIS OF LABOR IN YOUNG GIRLS

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AT HARLEM HOSPITAL, in New York City, 17,048 obstetric patients were admitted during the period from 1923 to 1933, inclusive. Of that large number, 100 were girls between the ages of twelve and fifteen. It was believed that a presentation of the course of labor and of infant and maternal morbidity and mortality would prove of interest.

The percentage of the cases in this young group to all obstetric cases in the ten-year period at Harlem Hospital is 0.58 per cent, or a ratio of 1 to 170.

Of the 100 young mothers, 2 were twelve years old, 10 thirteen years old, 26 fourteen years old, and 62 fifteen years old.

Ninety-nine of the 100 patients were primiparas. For 1932, 41 per cent (745 cases) of all obstetric cases in Harlem Hospital were primiparas, while 59 per cent were multiparas.

Ninety-three of the patients in our study were delivered in the hospital, while the remaining seven patients were delivered by outside physicians or midwives and brought to the hospital for postpartum care. These will be designated as Groups I and II, respectively. The term premature birth applies to newborn infants weighing between 1,500 and 2,500 gm.; miscarriage, to those weighing less than 1,500 gm.; and full term, to those weighing over 2,500 gm.

TABLE I. BIRTH STATISTICS AND MORTALITY

	GROUP I	GROUP II
Total number of babies	94	7
Full term {		
Livebirths	77	3
Stillbirths	2	1
Neonatal deaths	0	0
Premature {		
Livebirths	10	2
Stillbirths	0	0
Neonatal deaths	0	1
Miscarriages	5	1
Twin pregnancies	1	0

The total number of livebirths was 92 out of 101 for both groups, or 91.8 per cent. For the group which was delivered in the hospital, the ratio is 87 livebirths out of 94, or 92.6 per cent.

The average weight of 79 full-term babies was 6 pounds, 9½ ounces. The mean weight was 6 pounds, 8 ounces.

The ratio of the sexes of the babies born to the twelve- to fifteen-year group was 53 males to 41 females for the hospital deliveries. The ratio for all deliveries on the obstetric service in 1932 was 51 males to 49 females.

TABLE II. ANALYSIS OF UNCORRECTED FETAL AND NEONATAL MORTALITY

	12-15 YEAR GROUP 1923-33 101 BIRTHS		OBSTETRIC SERVICE, 1932					
			ENTIRE SERVICE 1658 BIRTHS		CLINIC 1210 BIRTHS		NONCLINIC 448 BIRTHS	
	NO.	%	NO.	%	NO.	%	NO.	%
Stillbirths								
Full term	3	2.98	18	1.85	15	1.23	3	0.67
Premature	0	0	48	2.89	22	1.81	26	5.80
Miscarriages	6	5.95	63	3.79	22	1.81	41	9.15
Total fetal mortality (full term and premature)	3	2.98	66	4.74	37	3.04	29	6.47
Total stillbirths	9	8.91	132	8.71	62	5.09	70	15.62
Neonatal mortality								
Full term	0	0	26	1.56	18	1.48	8	1.78
Premature	7	6.93	34	2.05	20	1.65	14	3.12
Previaible	0	0	23	1.39	6	0.49	17	1.40
Total neonatal mortality (full term and premature)	7	6.93	60	3.60	38	3.13	22	4.90
Fetal and neonatal mortality (full term and premature)	10	9.90	126	8.35	75	6.17	51	11.37
Total infant mortality	16	15.84	215	12.96	106	8.71	109	22.92

In analyzing the figures of fetal and neonatal mortality in Table II, we note that, while stillbirths at term were 60 per cent greater in the twelve- to fifteen-year group than in the entire obstetric service for 1932, premature stillbirths did not occur in the young group, while in the entire service there were 48 of 1,658 cases, or 2.89 per cent. These were mainly nonclinic emergency cases, 26 of 448 total cases, or 5.8 per cent. Miscarriages were 32 per cent more numerous in the young group than in the general service, the ratio being 5.95 per cent to 3.79 per cent. It will be seen that, of the nonclinic emergency cases, 9.15 per cent were delivered of miscarriages, while there were only 1.81 per cent miscarriages among the regular clinic cases. Total stillbirths were practically the same in both groups, 8.91 per cent for the young group and 8.71 per cent for the service. The regular clinic group, however, yielded 5.09 per cent stillbirths of the 1,210 births, while the nonclinic emergency group showed a stillbirth mortality of 15.62 per cent of 448 births.

The neonatal mortality for the young group was 6.93 per cent, all premature. This was three and a half times as high as the percentage of premature neonatal deaths for the entire obstetric service. The

figure was four and a half times that recorded for the regular clinic group, but only two and a half times higher than in the nonclinic emergency group.

Total infant mortality, including fetal mortality, miscarriages, and neonatal deaths, was 15.84 per cent for the young group, as contrasted with a mortality of 12.96 per cent for the entire service. For clinic cases, the percentage of infant mortality in the whole service was 8.71 per cent, and for nonclinic emergency cases, 22.92 per cent.

The Wassermann or Kahn test was made a routine part of the obstetric service in 1928. Of the 93 hospital deliveries in the young group, there is a report for 58 cases. With 1-, 2-, 3-, or 4-plus reactions regarded as positive, the percentage for the young group was 8.62 per cent, while the whole service yielded 309 positive reactions from 1,784 cases tested, or 17.32 per cent.

TABLE III. PRESENTATIONS

12-15 YEAR GROUP 1923-33		ENTIRE OBSTETRIC SERVICE 1932	
Total babies (including one twin pregnancy)	94	Total babies	1658
Vertex	92.55%	Vertex	93.10%
L.O.A.	57		
L.O.T.	1		
L.O.P.	1		
R.O.A.	24		
R.O.T.	2		
R.O.P.	2		
Breech	5.32%	Breech	6.09%
R.S.A.	3		
R.S.P.	1		
L.S.A.	1		
L.S.P.	0		
Undetermined	2		

TABLE IV. STATE OF PELVIS

12-15 YEAR GROUP 1923-33		ENTIRE OBSTETRIC SERVICE 1932	
Total cases	93	Total cases	1658
Ample	82.75%	Ample	87.5%
Deformed	17.25%	Deformed	12.5%

Antepartum complications for the twelve- to fifteen-year group totaled 16, or 17.22 per cent, while the total for the entire obstetric service for 1932 was 314 of 1,805 admissions, or 17.39 per cent.

The percentage of intrapartum complications in the twelve- to fifteen-year group was 13.98 per cent, or 12 of 93 cases. For the whole obstetric service in 1932, the incidence of intrapartum complications was 19.32 per cent, or 321 of 1,658 cases.

The operative incidence in the twelve- to fifteen-year group was practically the same as in the entire service for 1932. In the young group there were 87.2 per cent spontaneous and 12.8 per cent operative deliveries; for the service the figures are 87.5 per cent spontaneous and 12.5 per cent operative deliveries. These figures exclude episiotomies performed in both groups.

TABLE V. CONDITION OF PERINEUM

12-15 YEAR GROUP 1923-33		ENTIRE OBSTETRIC SERVICE 1932	
Total cases	93	Total cases	1658
Intact	67.74%	Intact	80.75%
First deg. lacer.	24.73%	First deg. lacer.	14.90%
Second deg. lacer.	6.45%	Second deg. lacer.	4.34%
Third deg. lacer.	0.0	Third deg. lacer.	0.06%
Episiotomies	9.74%	Episiotomies	6.80%

The incidence of postpartum complications in the young group was 23, or 24.7 per cent; and in the whole service, 23.5 per cent.

The incidence of morbidity in the young group was high. The guide used was the presence of a temperature of 100.4° F. for two days, exclusive of the first day. The ratio of morbidity was 21 cases in 93, or 22.6 per cent. The incidence of morbidity for the entire service in 1932 was 10.2 per cent of 1,658 cases.

For the young group, the fetal complications totaled 5, or 5.3 per cent of 94 infants. They included one case of spina bifida, one case of hallux valgus, and three cases of fetal distress.

In Table VI we have compared mortality rates for the twelve- to fifteen-year group with those for the entire service during 1932, divided into clinic and nonclinic cases. The maternal mortality per 10,000 livebirths has also been indicated. The figures in Table VI are

TABLE VI. MATERNAL MORTALITY

	CASES	DEATHS							NUMBER OF LIVE BIRTHS
		TOTAL		PUERPERAL		NON- PUERPERAL		PER 10,000 LIVE BIRTHS	
		NO.	%	NO.	%	NO.	%		
12-15 year group, 1923-33									
Delivered in hos- pital	93	3	3.2	3	3.2	0	0.0	345	87
Not delivered in hospital	7	0	0.0	0	0.0	0	0.0	0	5
Totals	100	3	3.0	3	3.0	0	0.0	326	92
Entire obstetric service, 1932									
Clinic cases	1331	12	0.9	9	0.67	3	0.22	104	1141
Nonclinic cases	474	8	1.6	6	1.26	2	0.42	206	378
Totals	1805	20	1.1	15	0.83	5	0.27	131	1519

in agreement with the findings of the Department of Labor for thirteen states in 1927, and for those states and two others in 1928. Their maternal mortality statistics are as follows: for colored females, 109 per 10,000 livebirths; for all females under fifteen, 161 per 10,000 livebirths; for colored females under fifteen, 235 for 10,000 livebirths.¹

As mentioned previously, there were seven patients who were delivered by others outside the hospital and brought there for postpartum care. These patients were all fifteen years of age. The puerperium was uneventful in two, parametritis occurred in one, morbidity in three, and cardiac complications in one. There were no maternal deaths in this group. The infant mortality is given in Table I.

The following are the case histories of the three patients who died postpartum. All were hospital deliveries.

M. S., a fifteen-year-old primiparous white female, was admitted to the obstetric service as a nonclinic emergency case on April 4, 1926. Labor had begun five hours and forty minutes before admission. When the patient was admitted, the fetal head was on the perineum. Ten minutes after admission, she was delivered of a normal child from an L.O.A. position; the child weighed 7 pounds, 14 ounces. The patient sustained a first-degree laceration of the perineum. Condition following delivery was good.

On admission, temperature was 100° F., and pulse 76. Urine was negative. Temperature was flat until the second day, when it suddenly rose to 101° F.; it reached 103° F. on the third day, and 104.4° F. on the fifth day, following which it dropped to normal and remained so until the seventh day. On that day the urine showed hyaline casts, a few leucocytes, and acetone, but no diacetic acid.

On the eighth day the temperature rose to 105.2° F. Blood culture on the same day revealed seven colonies of hemolytic streptococci per cubic centimeter, and on the ninth day 70 colonies of hemolytic streptococci per cubic centimeter within ten hours. The blood count on the tenth day showed 6,200 white cells, of which 70 per cent were polymorphonuclear leucocytes, and 30 per cent lymphocytes. On the eleventh day postpartum, blood culture showed 98 colonies of hemolytic streptococci per cubic centimeter within twenty-four hours.

The patient's temperature continued very high, and, despite three blood transfusions and continued stimulation, it rose to 107.8° F. on the thirteenth day postpartum, when the patient died.

Diagnosis: Septicemia (*Streptococcus hemolyticus*) and terminal bronchopneumonia.

B. S., a fifteen-year-old primiparous colored female, was admitted to the Obstetric Service of Harlem Hospital at 8:30 A.M. on March 7, 1925, as a nonclinic emergency case. The patient had been in labor for twelve hours prior to admission. Half an hour after admission, the patient was delivered spontaneously of a male child weighing 5 pounds, 8 ounces. She sustained a first-degree laceration of the perineum.

On admission, temperature and pulse were normal. On the third day postpartum, temperature suddenly rose to 103° F., and pulse to 140. Temperature continued between 103° F. and 105° F. until the twelfth day, when it dropped to 101.6° F., pulse 120.

On the fifth day postpartum, the patient began complaining of cough. The next day there was exquisite tenderness in both lower quadrants and foul lochia. Vaginal examination revealed induration of both fornices, tenderness, and heat in the vagina. Parametritis was diagnosed on the tenth day. On the twelfth day a diagnosis of

bronchopneumonia was made by the pneumonia service. After lapsing into unconsciousness, the patient died at 5:10 A.M. on March 19, twelve days postpartum.

Diagnosis: Bilateral parametritis and terminal bronchopneumonia.

M. B., a fifteen-year-old, single, primiparous, colored girl, was admitted to the Obstetric Service of Harlem Hospital on Jan. 8, 1931, at 8:35 P.M., with a history of having been in labor for forty-nine hours and thirty-five minutes. Pains were occurring every five minutes. The membranes had ruptured an hour before admission.

The patient had received adequate prenatal care. She had registered at the prenatal clinic on Sept. 4, 1930, and had made six antepartum visits in all. Her family, personal, and medical histories were all negative. The Wassermann reaction was likewise negative. The abnormal findings were breech presentation, umbilical hernia, and a generally contracted pelvis.

On admission, blood pressure was 110/54, temperature 99° F., pulse 88, respiration 22, fetal heart 150. The presenting parts were unengaged. Rectal examination revealed two and one-half fingers' dilatation of the cervix; no vaginal examination was made.

Approximately four hours after admission, the patient was delivered spontaneously of a living female child, weighing 6 pounds, 1 ounce. The second stage of labor lasted thirty-four minutes. There was a first-degree laceration of the perineum, which was sutured with one suture of No. 1 chromic catgut. The third stage of labor was prolonged, and the placenta was expressed one hour and twenty-four minutes after delivery. Hemorrhage was slight. The patient was given 1 c.c. of pituitrin at the end of the third stage.

On the third day postpartum, January 12, the patient began to complain of abdominal pain and vomiting. She vomited a huge amount of green fluid. The uterus was one finger below the umbilicus and very tender. The abdomen was markedly distended, with tenderness and rigidity over both lower quadrants. A diagnosis of parametritis and pelvic peritonitis was made. Temperature was 103° F., pulse 120, respiration 28, and blood culture negative. Abdominal puncture, made to rule out the possibility of pneumococcal peritonitis, showed streptococcus formation. Lung findings were negative. The patient was very toxic.

Vaginal examination on the ninth day revealed a dry mucous membrane and a relaxed perineum; the external os and the internal os each admitted the tip of a finger. The uterus was four fingers above the symphysis pubis. The abdomen was distended, and there were marked tenderness and rigidity over the umbilicus. Urine was negative. Blood count taken on the ninth day showed white blood corpuscles 19,400, polymorphonuclear leucocytes 82 per cent, lymphocytes 17 per cent, and transitionals 1 per cent.

On the tenth day postpartum the pulse ranged between 110 and 160. Temperature fluctuated between 100.2° F., and 105° F. Despite blood transfusions, elysis, and stimulation, the patient died on the eleventh day postpartum.

Diagnosis: Puerperal sepsis.

SUMMARY AND CONCLUSIONS

1. The ratio of births in the age group twelve to fifteen years in the years 1923-1933 to all births at Harlem Hospital, proved slightly higher than the ratio shown in the statistics of the Census Bureau for 1927. The incidence of primiparity for the young group was two and a half times that of the entire service at the Hospital, which, considering the age limits, is entirely logical.

2. The percentage of stillbirths at term was 60 per cent higher in the young group than in the whole service for 1932, and miscarriages were 32 per cent more numerous in the young group. However, premature stillbirths were nonexistent in the young group, and therefore the percentage of total stillbirths was practically the same in both groups. The percentage of neonatal deaths in the twelve- to fifteen-year group was three and one-half times as high as the figures for the whole service.

3. In the young group, birth weights of infants were half a pound less, on the average, than in the service proper for primiparas.

4. Positive Wassermann or Kahn reactions were half as frequent in the young group as in the general service. Evidently syphilis is acquired by the female later in life.

5. The ratio of vertex to breech presentations was practically the same in both groups. The percentage of ample pelves in the young group was lower, however, the ratio being 82.75 per cent to 87.50 per cent. The percentage of lacerated perineums was also definitely higher, due to the 99 per cent primiparas in the young group.

6. While antepartum complications were practically the same in both groups, intrapartum complications were 40 per cent lower in the twelve- to fifteen-year group. The operative incidence was the same for both groups. Postpartum complications were a trifle higher in the young group.

7. Morbidity was more than twice as high in the young group as in the entire service. This is a disquieting factor and shows less fitness for pregnancy in the young group (as might be expected from the age limits twelve to fifteen) than is possessed by the older group in the service.

8. In comparing maternal mortality in the young group with maternal mortality in the entire service for 1932, it should be remembered that the ratio of patients was 100 to 1,805. On the basis of these figures, the mortality of the young group was three times that of the general service. In addition, all deaths in the young group were in the acute emergency cases.

9. It should be noted that all three deaths in the young group followed spontaneous deliveries, and that there were no postoperative deaths.

10. The importance of prenatal care should also be noted, for two of the three patients who died postpartum received no antepartum care.

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TREATMENT OF THE PERSISTENT OCCIPITOPOSTERIOR POSITION BY 180 DEGREE MANUAL ROTATION OF THE OCCIPUT

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IT IS only too well known to those who practice obstetrics that the persistent occiput posterior and to a lesser degree the persistent occiput transverse are very frequent causes of maternal exhaustion, fetal embarrassment and delayed delivery.

The incidence of posterior position is given as less than 1 per cent by Tweedy¹ in 13,511 deliveries, while Williams² reports 11.3 per cent in 5,000 cases. In 2,365 cases Piper³ found an incidence of 17.1 per cent, which also included occiput transverse positions. At the Philadelphia Lying-In Hospital, Piper noted an incidence of 29 per cent.

If all patients were examined by experienced attending obstetricians at the onset of labor instead of by internes, the figures quoted in the preceding paragraph would undoubtedly be found far too low. Percentages for the incidence of the posterior and transverse positions at the commencement of labor will have to be enormously increased since the thorough anatomic researches by Caldwell, Moloy and D'Esopo.⁴ They have proved by x-ray that the great majority of labors begin as occiput posterior or occiput transverse.

It is probable that in the vast majority of cases, the occiput, at the commencement of labor, is either transverse or posterior. In most of these patients anterior rotation takes place and delivery is spontaneous. Interference is necessary only in those cases where anterior rotation fails to take place and where the occiput persists in remaining either posterior or transverse.

In a small percentage of cases the occiput is delivered posteriorly. In these cases birth is either spontaneous or is effected by forceps. There are several methods of coping with or correcting these positions. Most of them are efficient and not very hard to master.

Since these cases are very likely to be long and drawn out, practically all authorities are agreed that watchful waiting and some sort of analgesia is the proper treatment for the first stage of these labors. During this stage some advise that the patient lie on that side toward which the fetal back is directed, thereby favoring anterior rotation. Some claim good results with tight abdominal binders.

After the cervix is fully dilated or fully dilatable various means are employed to hasten or effect delivery, by internal podalic version, the

Scanzoni or the modified Scanzoni maneuver. The Kjelland and, to a lesser degree, the Barton forceps are used by some, especially in persistent transverse positions. Manual rotation of the head has been found successful by a few and some textbooks recommend it.

The Pomeroy maneuver was introduced by the late Ralph Pomeroy of Brooklyn. Unfortunately, he never published the procedure. The only reference in the literature to the Pomeroy maneuver is a paper entitled "The Pomeroy Maneuver in the Treatment of the Persistent Occipitoposterior Position," by Aranow.⁵

The Pomeroy maneuver consists in rotating the posterior fetal shoulder. The rest of the fetus follows this rotation. In order to prevent the head from rotating back again to its original position, he advised and practiced overcorrection, i.e., from R.O.P. to L.O.A. and from L.O.P. to R.O.A. The transverse positions are similarly overcorrected, i.e., R.O.T. to L.O.A. and L.O.T. to R.O.A. This rotation can be performed as soon as the cervix is sufficiently dilated to admit the whole hand. It was Pomeroy's custom to perform anterior rotation and then leave the case to nature.

Pomeroy and Aranow report excellent results from this procedure. I have personally performed the Pomeroy maneuver many times and I can attest to its efficacy.

After some experience with rotation I found that it was not necessary to rotate the shoulder; that the rotation of the head alone would safely effect the change from a posterior or transverse position to an anterior. The best results, however, are obtained when rotation of the head is done by minutely following the technic as worked out by Pomeroy in his shoulder rotation. I have tried rotation by ordinary methods and found that it is far inferior to the Pomeroy method. Manual rotation of the head when performed in a manner similar to Pomeroy's shoulder method will immeasurably facilitate rotation and will greatly lessen the complications and dangers of the persistent occiput posterior and transverse positions.

TECHNIC

Unless there is an emergency no interference is practiced until the cervix is fully dilated. If, after full dilatation, delivery is deemed advisable, the patient is anesthetized, preferably with ether, and placed in the lithotomy position. The bladder is emptied by catheter and the perineum is "ironed out" with tincture of green soap.

In R.O.P. and in R.O.T. the operator faces the patient's right thigh, bends both knees as much as is necessary, and acutely bends his body at the waist sharply to the left. He then inserts his whole right hand into the vagina and the forearm is pronated so that the thumb is below and

posterior and the other four fingers above and anterior to the fetal head. The operator then slowly assumes the erect posture and as he does so he supinates his forearm thus forcing the occiput to rotate 180 degrees in the case of occiput posterior and in either case converting the position into an L.O.A.

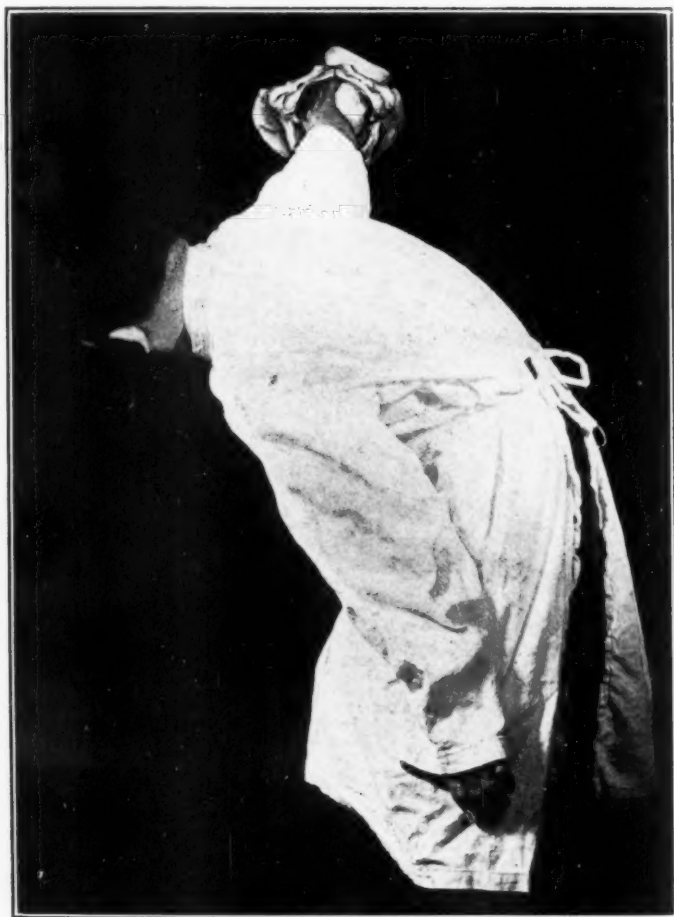


Fig. 1.—Showing first position of operator in effecting rotation.

In L.O.P. and in L.O.T. the operator faces the patient's left thigh, bends his knees as above, and acutely bends his body at the waist to the right. He inserts his whole left hand into the vagina and proceeds as above described, rotating the head into the R.O.A. position as he straightens his body and supinates his forearm.

After completion of the rotation, which rarely takes more than half a minute, a nurse or an assistant exerts pressure on the fundus until the forceps are applied. While advisable, this procedure is not essen-

tial. I have frequently performed rotation where no assistant or nurse was available, fundal pressure was not employed, and the head rarely rotated back to either its former or the corresponding anterior position. Should the head rotate back to or toward its former position, the maneuver is simply repeated. A cephalic application of the type of forceps to which the operator is accustomed is then made and delivery effected in the usual manner.

The contraindications to this procedure are appreciable contractions of pelvis and disproportion. In cases of this sort where vaginal delivery is considered reasonably possible I prefer internal podalic version.

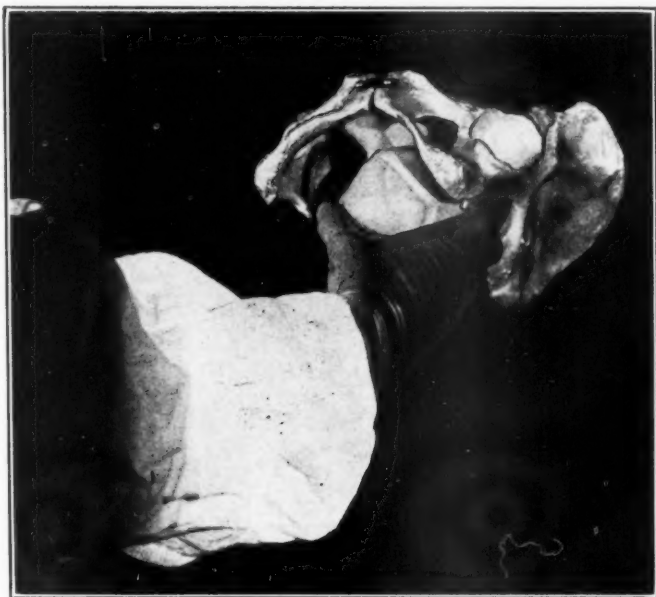


Fig. 2.—Showing second position.

I have frequently displaced the head rather high while performing the maneuver, but since I perform rotation only in fairly normal pelvis I found that this high displacement made very little difference in the delivery. Whereas I would under no circumstances apply high forceps in contracted pelvis, I do not hesitate to do so in these cases. In some of these cases where the head was unduly displaced I performed podalic version from choice and not of necessity.

I have delivered 146 patients by this modified Pomeroy technic. I never failed to effect rotation. However, in a few cases, because of disproportion, I was unable to deliver by forceps after rotation. These patients I delivered by podalic version. These latter cases are not included among the 146 in this report.

TABULATION OF CASES			
PARA O	PARA I	PARA II	PARA III
113	22	9	2
R.O.P.	R.O.T.	L.O.P.	L.O.T.
95	8	37	6

In one case the patient was allowed to deliver spontaneously after completion of the rotation. Two cases were delivered as posterior.

In six cases I was called after the attendants had unsuccessfully attempted delivery with forceps. In every case delivery was either easy or fairly easy after rotation. There were no maternal deaths.

There were three fetal deaths. In two of these cases I could hear no heart sounds when the family doctor called me to deliver the patients. In one case the labor had lasted four days, and in the other case labor had lasted over two days, and the doctor had made several attempts on different occasions to effect delivery with forceps. The third case was also one of prolonged labor, and the family doctor had unsuccessfully tried forceps delivery at the patient's home. The baby lived for one day after delivery. Death was in all probability due to cerebral hemorrhage. No autopsy could be obtained.

There were four cases of Erb's palsy. They were all of the mild variety and cleared up in a short time.

CONCLUSION

The 180 degree manual rotation of the occiput is one of the most efficient if not the most efficient method of treating persistent occipito-posterior or transverse positions.

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1882 GRAND CONCOURSE

Ito, Sh.: *Mastitis and Puerperal Psychosis*, *Jap. J. Obst. & Gynec.* 17: 373, 1934.

Ito maintains that infection due to trauma during delivery often leads to puerperal psychosis. Other causes of puerperal psychosis are intense pruritus, carbuncles, mastitis, pneumonia, etc. The occurrence of puerperal psychosis following mastitis is rare and the author reports such a case. The psychosis disappeared shortly after the abscess was incised and drained. The patient has remained well. The most important immediate cause of the psychosis was the bacterial toxin from the breast abscess. Contributing factors were individual predisposition, the puerperium and fear, also pain and fever associated with the mastitis.

J. P. GREENHILL.

THE RESULTS OF TREATMENT OF BENIGN LESIONS OF THE CERVIX UTERI

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THE results of treatment of non-neoplastic diseases of the cervix uteri in the Hospital of the University of Pennsylvania are reported in this paper. The study is confined to three topics: (1) relief of leucorrhea, (2) conception subsequent to cervical repair, and (3) incidence of carcinoma following repair.

SOURCE OF DATA

About 18 per cent of the patients admitted to the Hospital Service of the Department of Gynecology between 1899 and 1934 received treatment for cervical lesions. Of the 4,050 patients so treated, 18 per cent (741 patients) had malignant, and 82 per cent (3,309 patients), benign diseases of the cervix. The patients treated for carcinoma of the cervix have been reported upon by Norris¹ and by Keene and Kimbrough.² The present study of the benign lesions is based upon information gathered partly by follow-up examination but largely from questionnaires returned by 600 patients treated for cervical diseases in the twenty years from 1914 to 1934. Thirty-three per cent of 1,800 questionnaires were answered. (This is the usual return for questionnaire studies on this subject; Rawls³ 30 per cent, Leonard⁴ 32 per cent, Bullard⁵ 38 per cent.) Of the 600 answers, 58 per cent were from ward and 42 per cent from private patients. The approximate proportions of all patients admitted to the department are 65 per cent ward and 35 per cent private. The files of the department contain recent information on eleven additional patients, making a total of 611 patients traced. The average age of the patients when treated was thirty-nine years, and when traced by questionnaire forty-seven years, making the average period of follow-up eight years.

PURPOSE OF TREATMENT

The purpose of treatment of the cervix was (1) relief of abnormal discharge, (2) eradication of cervical infection, (3) anatomic restoration of the cervix. An additional consideration was the extirpation of potentially malignant tissue. The prophylactic effect of cervical surgery against subsequent carcinoma is of especial interest, as will appear below. Treatment of the cervix was not undertaken for the pur-

pose of relieving backache, abdominal pain, or dysmenorrhea (except that due to cervical obstruction). No patient in the present series who received treatment of the cervix alone was relieved of backache or abdominal pain. This observation supports Fulkerson's⁶ opinion that uncomplicated cervicitis does not cause backache.

INDICATIONS FOR EACH TYPE OF TREATMENT

Since all the patients were admitted to the hospital, it was possible to undertake any operative treatment of the cervix which was indicated. Minor degrees of erosion, endocervicitis, and cystic cervicitis were treated by cauterization, usually under anesthesia. Occasionally, to save time in a case requiring extensive abdominal surgery, the cervix was treated by cauterization rather than by a more time-consuming method which might otherwise have been preferable.

Cervices presenting marked anatomic defects such as deep laceration and eversion, extensive endocervicitis or cystic changes, were treated by Sturmdorf's operation or by amputation. In recent years the Sturmdorf stitch has been used for covering the stump after amputation.

In general the operation of choice was that which promised to eradicate infection and to restore the cervical contours most effectively. The effect upon subsequent childbirth was a secondary consideration, for it was believed that the principal problem was improvement of an existing condition rather than provision for a future contingency. However, in treating patients in the childbearing age a minimum of cervical tissue was removed. In older women more extensive excision was practiced.

The 611 patients included in this study were operated upon by one of a staff of six men formerly headed by, and still influenced by, Dr. John G. Clark. Adherence to his principles has maintained in the present staff an exceptionally uniform system of treatment of cervical lesions, which may account, in part, for the uniformity of the results obtained.

EFFECTIVENESS OF VARIOUS METHODS IN THE TREATMENT OF LEUCORRHEA

By following up 171 patients treated in this clinic, Payne⁷ found that all methods of treatment (cauterization, trachelorrhaphy, Sturmdorf operation and amputation) gave approximately the same percentage of relief from leucorrhea when the choice of treatment was governed by the considerations outlined above. He concluded that effective treatment of leucorrhea depends mainly upon the selection of a type of treatment appropriate to the individual case. Surgical judgment seemed to him of greater importance than surgical technic. The present study of 611 patients (including Payne's) supports his beliefs. Each of the four methods studied gave *relief* in approximately 84 per cent of patients so treated (Table I).

TABLE I. COMPARISON OF RESULTS OF DIFFERENT TREATMENTS FOR LEUCORRHEA (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	TOTAL		TOTAL CURED OR IMPROVED	CURED	IMPROVED	NOT IMPROVED
	PATIENTS	PER CENT				
Cauterization	185	100	86%	80%	6%	14%
Trachelorrhaphy	90	100	83%	70%	13%	17%
Sturmdorf	135	100	84%	80%	4%	16%
Amputation	48	100	85%	83%	2%	15%
Final results from all methods of treatment	458*	100	84%	78%	6%	16%

*None of these patients received gynecologic treatment, or conceived during the period of follow-up.

It will be noted that trachelorrhaphy gave the lowest percentage of *complete cures*, as might be expected of a procedure which does not remove all the infected endocervix. Moreover, trachelorrhaphy was the slowest treatment in effecting cure (Table II).

TABLE II. INTERVAL BETWEEN TREATMENT FOR LEUCORRHEA AND CURE (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)*

	TOTAL		INTERVAL IN MONTHS			
	PATIENTS	PER CENT	0-1	2-3	4-11	12 AND OVER
Cauterization of the cervix	98	100	43%	35%	11%	11%
Trachelorrhaphy	41	100	32%	27%	21%	20%
Sturmdorf operation	63	100	48%	30%	11%	11%
Amputation of the cervix	23	100	35%	35%	13%	17%
All treatments	225	100	42%	32%	13%	13%

*It will be noted that of those patients who were completely cured of leucorrhea, in three months, 78 per cent were cured by the cautery, 78 per cent by Sturmdorf, and 70 per cent by amputation but that, in the same period, trachelorrhaphy had accomplished a cure in only 59 per cent.

RESULTS IN THE TREATMENT OF LEUCORRHEA

Leucorrhea was present in 85 per cent of our 611 patients who required treatment of the cervix. (It was present in 74 per cent of Fulkerson's⁶ series, 80 per cent of Sovak's,⁸ and 85 per cent of Leonard's.⁴)

Payne's⁷ studies in 1929 showed that approximately 96 per cent of 171 patients who had been treated for leucorrhea in this clinic were cured or improved. His follow-up period was one to five years, and the results he reported were as good as those published elsewhere. The present series shows 84 per cent of patients cured or improved. This percentage of relief of leucorrhea, which is lower than Payne's or most other authors' (Table III) may be accounted for by the longer period of follow-up in the present series (one to twenty years). During that period the early good results may have been modified by infection (gonococcus, trichomonas vaginalis), childbirth, prolapsus uteri, subsequent

operation, etc. Allowance has been made for these factors when known. Although approximately 15 per cent of patients who were treated for leucorrhea were not improved, this does not necessarily indicate a poor anatomic result, for Fulkerson⁶ found that 14 per cent of patients whose cervixes had healed satisfactorily after repair still complained of leucorrhea.

Data from the present series are not available for a study of the causes of failure to cure leucorrhea.

TABLE III. RESULTS OF TREATMENT FOR LEUCORRHEA

AUTHOR	NUMBER OF PATIENTS TREATED	TOTAL CURED OR IMPROVED	PER CENT			
			CURED	IMPROVED	NOT IMPROVED	TOTAL
<i>Antiseptics and Caustics</i>						
Fulkerson ⁶	423	82%	12	70	18	100
<i>Cauterization of the Cervix</i>						
Fulkerson ⁶ (no anesthetic used)	524	98%	74	24	2	100
Matthews ⁹ (no anesthetic used)	226	100%	80	20	0	100
Matthews ⁹ (anesthetic used)	55	84%	51	33	16	100
Tompkins* (anesthetic usually used)	185	86%	80	6	14	100
<i>Trachelorrhaphy</i>						
Bullard ⁵	50	74%	—	—	—	—
Rawls ³ (cervical repair only)	66	83%	44	39	17	100
Rawls ³ (cervical and vaginal repair)	35	72%	34	38	28	100
Leonard ⁴	33	84%	42	42	16	100
Tompkins*	90	83%	70	13	17	100
<i>Sturmdorf Operation</i>						
Bullard ⁵	53	92%	—	—	—	—
Burns ¹⁰	92	97%	—	—	—	—
Wolfe ¹¹	130	97%	79	18	3	100
Sovak ⁸	75	93%	88	5	7	100
Matthews ¹²	200	92%	64	28	8	100
Matthews ⁹	70	93%	70	23	7	100
Tompkins*	135	84%	80	4	16	100
<i>Amputation of the Cervix</i>						
Bullard ⁵ (high amputation)	39	100%	—	—	—	—
Bullard ⁵ (low amputation)	99	88%	—	—	—	—
Leonard ¹³	109	93%	63	30	7	100
Rawls ³ (amputation only)	128	92%	61	31	8	100
Rawls ³ (amputation and vaginal repair)	77	90%	57	33	10	100
Tompkins*	48	85%	83	2	15	100

*Data assembled for present report.

CONCEPTION SUBSEQUENT TO TREATMENT OF THE CERVIX

It is the opinion of some gynecologists that conception is less likely to follow amputation than other cervical operations (Table IV). In our series approximately two-thirds of all patients who were likely to conceive did so regardless of the type of treatment of the cervix (Table V).

TABLE IV. PERCENTAGE OF PRESUMABLY FERTILE WOMEN WHO CONCEIVED SUBSEQUENT TO TREATMENT OF THE CERVIX

AUTHOR	LEONARD	RAWLS	SOVAK	BURNS
Length of follow-up	1-20 YEARS	1-5 YEARS	2-3 YEARS	2 YEARS
Number of presumably fertile women	101	149	54	65
Trachelorrhaphy	38%	42%	—	—
Sturmdorf operation	—	—	66%	22%
Amputation of the cervix	20%	28%	—	—

TABLE V. PREGNANCY SUBSEQUENT TO CERVICAL TREATMENT OF 256 WOMEN* WHO HAD PREVIOUSLY BORNE CHILDREN (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	TOTAL		NOT PREGNANT SUBSEQUENTLY	PREGNANT SUBSEQUENTLY
	PATIENTS	PER CENT		
Cauterization of the cervix	75	100	37%	63%
Trachelorrhaphy	80	100	29%	71%
Sturmdorf operation	83	100	28%	72%
Amputation of the cervix	18	100	39%	61%
Pregnancy subsequent to all treatments	256	100	32%	68%

*Widows, divorcees, women over forty, women not menstruating regularly, women treated by radium or surgical sterilization, not included.

When nulliparous married women were considered, it was found that approximately half of those who received no operative treatment except treatment of the cervix later conceived (Table VI).

From the data available it is not possible to determine whether cervical repairs, by producing stenosis, decrease the chance of subsequent con-

TABLE VI. PREGNANCY SUBSEQUENT TO CERVICAL TREATMENT OF 25 PRESUMABLY FERTILE* MARRIED WOMEN WHO HAD NEVER BEEN PREGNANT (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	TOTAL PATIENTS	NOT PREGNANT SUBSEQUENTLY	PREGNANT SUBSEQUENTLY
Cauterization of the cervix	22	9	13
Trachelorrhaphy	1	1	0
Sturmdorf operation	2	1	1
Total	25	11	14
	100%	44%	56%

*Widows, divorcees, women over forty, women not menstruating regularly, women treated by radium or surgical sterilization not included.

ception. In the first place, many patients do not submit to repairs until their families are completed. Further, many patients are advised not to bear children after a plastic repair; and a few in whom repairs have been extensive, are warned that future pregnancy should be terminated by cesarean section. Therefore, as Rawls³ pointed out, the voluntary sterility of women tends to increase after repair of the cervix.

The same factors also influence the incidence of voluntary abortion and miscarriage among women who become pregnant after repairs. Therefore we have made no attempt to study the effect of such treatment as regards predisposition to miscarriage.

Reliable information is not available for a study of dystocia and premature labor subsequent to cervical repair in this series of patients.

INCIDENCE OF CARCINOMA AFTER CERVICAL REPAIR

In studying the value of cauterization and other treatments of the cervix as prophylaxes against carcinoma, the closest scrutiny must be

TABLE VII. CARCINOMA SUBSEQUENT TO TREATMENT OF BENIGN LESIONS OF THE CERVIX (HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA)

	NUMBER OF PATIENTS	AVERAGE AGE WHEN TREATED	AVERAGE AGE WHEN FOLLOWED UP	AVERAGE FOLLOW-UP PERIOD	SUB- SEQUENT CERVICAL CARCINOMA
Cauterization	228	37.0	43.0	6.0 years	0
Trachelorrhaphy	116	34.5	44.5	10.0 years	1
Trachelorrhaphy and light cauterization	10	36.5	43.5	7.0 years	0
Sturmdorf operation	180	41.5	49.0	7.5 years	1
Amputation	77	44.5	55.0	10.5 years	0
Totals	611	39.0	47.0	8.0 years	2

This table is based upon a follow-up of 611 patients treated between 1914 and 1934. Attempts to trace 1,200 additional patients treated in the same period were unsuccessful, but none of them is known to have developed carcinoma of the cervix. The Sturmdorf operation and cauterization were not regularly employed until after 1920, which accounts for the shorter follow-up period in groups treated by these methods. The table shows the tendency to use the Sturmdorf operation or amputation in older patients.

Brief abstracts of the histories of the two patients who developed carcinoma are given:

CASE 1.—M. B., para iii, trachelorrhaphy at twenty years of age. No pathologic report on the tissue removed. Pelvic symptoms were relieved for twenty years. No pregnancy subsequent to cervical repair. At twenty-six a radical mastectomy was performed for scirrhus carcinoma (histologic diagnosis) in the Hospital of the University of Pennsylvania (Surgical Records 62: No. 8528). At the age of forty, metrorrhagia developed. Stage III cancer of the cervix was discovered. Biopsy showed epidermoid carcinoma (Gynecologic No. 14192).

CASE 2.—F. S., para iii, Sturmdorf operation at thirty-three years of age for leucorrhea. Microscopic examination of tissue removed showed no carcinoma. No subsequent pregnancy. The leucorrhea was not relieved. Total hysterectomy at thirty-eight years of age. No clinical evidence of carcinoma but routine histologic examination of the uterus showed epidermoid carcinoma in the cervical portion (Gynecologic No. 22966).

focused upon the favorable statistics which have previously been published. Attention should be directed to the percentage of patients followed, the length of the follow-up, and the average age of the patients. In evaluating the accumulated statistics of several authors, the student must be certain that there is no "overlapping" of the cases tabulated.

In the present study questionnaires were mailed to 1,800 patients treated in this clinic between 1914 and 1934 for benign lesions of the cervix. Microscopic examination of the tissue removed by cervical repair did not show carcinoma in any instance. Six hundred patients were traced by questionnaire. In addition eleven patients have recently reported to the department. Two of these patients have developed carcinoma of the cervix subsequent to cervical repair (Table VII). It should be noted that most of the patients listed in Table VII have not recently been examined, so that it is possible that some of them have cervical carcinoma at the present time without our knowledge.

SUMMARY

1. Six hundred and eleven patients treated for benign cervical lesions at the Hospital of the University of Pennsylvania between 1914 and 1934 were traced.

2. The methods of treatment were cauterization, trachelorrhaphy, Sturmdorf operation and amputation. The indications for each are outlined.

3. Each method gave *relief* of leucorrhea in approximately 85 per cent of cases.

4. Trachelorrhaphy gave a lower percentage of *complete cure* of leucorrhea and effected cure more slowly than other methods.

5. Statistics from other clinics on the relief of leucorrhea have been tabulated for comparison.

6. Approximately 66 per cent of married women in the childbearing age who had previously borne children conceived after each type of cervical repair.

7. Approximately 50 per cent of married women in the childbearing age who had never been pregnant conceived after cervical repair.

8. The tendency of cervical repair to increase voluntary sterility and abortion is discussed.

9. Two patients among 611 who were traced after the repair of benign lesions of the cervix subsequently developed cervical carcinoma.

CONCLUSIONS

1. The most important factor in the relief of leucorrhea due to cervicitis is the selection of a type of treatment suitable to the individual case. Approximately 85 per cent of patients will be *relieved* of leucorrhea if the choice of treatment is based upon the indications outlined.

2. In general, trachelorrhaphy cannot be recommended as a satisfactory procedure when the principal object of treatment is *complete cure* of leucorrhœa.

3. The possibility of producing cervical stenosis which will interfere with conception should not influence the choice of treatment for benign lesions of the cervix.

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COMPLICATIONS FOLLOWING CAUTERIZATION OF THE CERVIX UTERI

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THE use of the electrocautery in the treatment of diseases of the cervix uteri is far from being a harmless procedure and may produce serious infection. The feeling has arisen, unfortunately, that no complications need be feared in routine use of the cautery. The application of the cautery in the treatment of endocervicitis and other lesions of the cervix was first suggested by Byrne in 1892, and has become an exceedingly common procedure. The method, originated in its present form by Hunner in 1906, has become most convenient and popular in the management of even very severe erosions and eversions.

The ease with which the method may be applied and the excellent results obtained almost painlessly in office practice or under anesthesia in the operating room, almost universally, has had the effect of minimizing any apprehension on the part of those employing cautery treatment. Abnormal epithelium is destroyed, deep infection is checked, followed in the majority of cases by epithelialization of the cervix and complete cure of the lesion, without surgical operation or prolonged treatment.

There are many modifications of cautery tips, viz., the nasal cautery suggested by Dickinson, the Cherry, Ende, and Hyams types. The electrocautery is very effective in treating cysts of endocervicitis, cervical polyps, and all types of erosions. Curtis advises against the heavy duty or Paquelin cautery. Masson and Parsons have reported great effectiveness of the cautery in all types of leucorrhea in which infection of the cervix is the etiologic factor.¹ Holden has described in detail the method of treating high cysts with marked dilatation of the cervical canal effectively with cautery.² Its use is advocated also in the treatment of obstinate gonorrheal infections where it may be of service in destroying the primary stubborn foci which produce persistent reinfection, and its use is suggested (Curtis) between attacks of acute salpingitis to prevent subsequent exacerbations by eliminating persistent foci.³ The contraindications and dangers of cautery treatment, however, have not been sufficiently emphasized. Curtis recently has stated "reticence in discussing unfavorable results has perhaps tended to conceal the *true incidence of complicating cellulitis*; nearly all with whom I have discussed this subject state that they have had cases of pelvic cellulitis in patients subjected to endocervical cauterization." He emphasizes also the important observation that the danger is augmented in cases of displacement where there is interference with good mechanical drainage from the uterus and necrotic infected material stagnates within the uterine canal. Masson and Parsons report three cases of pelvic abscesses occurring in their series of cases.

We have observed recently a number of complications following cauterization, three of which are reported here.

The complications occurring in our hands have followed cauterizations after the heavy duty cautery, or the Postcautery in office practice. Very light surface cauterization with the finer types of cautery is definitely advisable but is less effectual.

CASE 1.—This patient, a white woman of twenty-six, para 0, was admitted to the Lakeside Hospital, July 1, 1933, complaining of profuse and irregular menstruation of several months' duration. Pelvic examination revealed nothing of note at that time except a marked erosion of the cervix. Smears were negative. A diagnostic curettage was performed and the cervix was cauterized. This patient was readmitted two weeks later complaining of severe bilateral abdominal pain, nausea, and vomiting. There was moderate fever and irregular spotting. A definite mass could be felt on the right side, and there was marked bilateral tenderness, and a tubal pregnancy being suspected, laparotomy was performed after three days' observation. Laboratory findings were consistent with acute salpingitis. Old blood was obtained on culdesac needle puncture. The gross findings at operation were those of acute salpingitis, both tubes being sealed off and swollen markedly. There were a few old clots in the culdesac. Bilateral salpingectomy was performed. Microscopic examination revealed an ectopic gestation in the right tube, which was adherent to the ovary, and subacute bilateral salpingitis. The postoperative course was uneventful and patient was discharged July 30, 1933 convalescing satisfactorily. The ectopic pregnancy was incidental obviously but the acute tubal inflammation seemed definitely to have been initiated by the cauterization.

CASE 2.—This patient was a twenty-one-year-old nullipara, who was admitted to Lakeside Hospital, March 21, 1933, complaining of backache and pain in the left side, with vaginal discharge of three months' duration. The past history was negative except for appendectomy and oophorectomy in 1931 (presumably an attack

of salpingitis). Family history and marital history otherwise essentially negative. Menstrual history negative except for an abortion in 1932, without infection, as far as could be ascertained from the history.

Physical examination was not remarkable. Pelvic examination showed a marital outlet in good condition. The cervix was markedly eroded, the uterus was in deep midposition, only fairly movable, and there were no lateral masses made out. The cervix was dilated. It was markedly hypertrophied and contained numerous large infected nabothian follicles. The cervix was cauterized thoroughly under anesthesia and a Smith-Hodge pessary was inserted to give the uterus a better position for drainage. The patient was discharged on her second postoperative day without an elevation of temperature. One week later she complained of soreness in both lower quadrants, which persisted until her admission to the hospital April 12, 1933. Physical examination at this time revealed a moderately ill white woman with the usual signs of toxemia. There was marked tenderness in both lower quadrants with some spasticity. Pelvic examination revealed a cervix still acutely inflamed from cauterization, and the uterus was small and anterior; there was a large mass in the culdesac. Her temperature was 38.8° C., pulse 90, and respirations 22. The white blood count was 7,650. Sedimentation tests showed moderate activity.

A posterior colpotomy was done on her first hospital day and 500 c.c. of foul-smelling pus evacuated. Temperature immediately fell to normal and she was discharged on her seventh postoperative day in good condition. It is impossible to say whether the cauterization lighted up a latent infection persisting, perhaps, from the abortion or an old salpingitis, or whether the abscess was metastatic from the badly infected cervix.

CASE 3.—This patient was admitted to Lakeside Hospital, March 13, 1934, complaining of constant vaginal discharge with lower abdominal pain since October, 1933, at which time she had had an induced abortion. She was suspected of having an ectopic pregnancy as she complained of severe abdominal pain and faintness shortly before her admission to the hospital. Her past two periods had been prolonged but were otherwise normal. Aschheim-Zondek test was negative. Smears from the cervix were negative.

Her anamnesis was unessential. Physical examination was essentially negative except for the pelvis which showed normal external genitalia, a markedly eroded cervix, and a fundus in retroversion pulled slightly to the left. No abnormal lateral masses were felt. Laboratory findings revealed nothing of note. On her second hospital day a dilatation and curettage were done. The scrapings showed interval endometrium. The cervix was cauterized, and the fundus was replaced and held anteriorly by a Smith-Hodge pessary. She was discharged March 15, 1934 in good condition.

She returned to the dispensary March 21, 1934 complaining of abdominal pain and soreness, which grew worse with exercise. Pelvic examination was negative except for some sloughing of the cervix and lower abdominal tenderness. She returned again April 4, 1934 with similar complaints and more obvious physical findings with marked tenderness in both fornices, which was more marked on motion of the cervix. She returned again April 13, 1934, complaining of much more pain and vaginal bleeding. She was not examined at this time. She made five subsequent visits to the dispensary, the last, June 27, 1934, when she complained at this time of severe dysmenorrhea, and moderate backache with profuse bleeding at her last period, at which time the fundus was in mid- to anterior position, bilateral masses were present in the fornices, the larger of which was in the left fornix and measured 5 by 7 cm.

in diameter, and both fornices were exquisitely tender. She was still undergoing Elliott treatment three months later with marked regression of her cellulitis. The immediate response in the form of a pelvic flare-up strongly suggests that a part was played in its etiology by the cauterization.

The occurrence of widespread pelvic infections following cauterization is evidently much more frequent than is commonly supposed. The presence of a latent gonorrheal infection of the cervix should be carefully eliminated wherever possible. Patients with a history of infected abortion, especially of recent occurrence, should be dealt with most cautiously as subjects for cervical cauterization especially with the heavy duty or Paquelin cautery. Since these cases, we have had under observation recently an instance of pelvic inflammatory disease, apparently immediately initiated by office cauterization for erosion of the cervix in a patient with adherent retroversion of the uterus and one-child sterility of seven years' duration. This patient had had a number of negative smears and had no local stigmas of gonorrhea. These cases suggest that the cautery should be employed with extreme care and circumspection and with the knowledge that severe cellulitis may result occasionally as a complication.

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The amount of fibrinogen in the blood of healthy children at birth seems to be low; it then rises rapidly to something above 2 per cent after a week. This rise in the first few days after birth cannot be occasioned by loss of water alone, as the amount of serum albumin, and consequently of water also, seems to undergo no change.

In the sick children which the author examined, particularly in those exhibiting an increased tendency to bleeding, this rise in the amount of fibrinogen in the blood seemed to be absent, the values generally remaining lower than in healthy children of corresponding age. Also the power of coagulation of the blood was considerably lowered in these children. The low amount of fibrinogen and the lowered power of coagulation in the blood of children suffering from hemophilia neonatorum temporaria probably are to be regarded as causative of this condition, although other factors, as for example a change in the amount of calcium and fluorid contained in the blood, and also its degree of oxygenation, may play a certain part. After transfusion of blood the amount of fibrinogen is increased, and also the power of coagulation of the blood, which circumstance may possibly explain the favorable effect of blood transfusion on children with a heightened tendency to bleeding.

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THE SEX PREDICTION TEST OF DORN AND SUGARMAN

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DORN AND SUGARMAN, in 1931, while investigating the possibility of utilizing male rabbits for the Aschheim-Zondek method of diagnosing pregnancy, observed that singular differences in the testicular response became apparent following the injection of urine from pregnant women. These differences were ascribed to hormones dependent on the sex of the unborn child. By injecting immature rabbits with urine of women in the fifth to tenth months of pregnancy, these authors were able to correctly foretell the sex of the unborn child in 80 out of 85 cases. Urine from women carrying female children was found to stimulate the testes to precocious development as evidenced by grossly recognizable enlargement and congestion, as well as by microscopic signs of accelerated spermatogenesis. This stimulation was not observed when the injected urine came from women bearing male children. The importance of using suitable test animals was emphasized by these authors. For satisfactory results, it was found that the testes of the rabbits must already be through the inguinal rings, but not yet in the scrotum. In the event that the testes had not yet descended into the canal, they would not react to the injection, presumably due to their immaturity. On the other hand, after the testes had reached the scrotum, spermatogenesis had already been so well established that no further response could be elicited. These authors found that a relationship exists between the stage of descent of the testes and the development of spermatogenesis. This fact, according to them, obviates the need for controls. In 1933 Curphey and Romer described a spermatogenic factor in the urine of pregnant women, but this factor was apparently unrelated to the sex of the unborn child. They used a pure strain of rabbits and concluded that the anatomic position of the testis at the time of the injection of the urine of pregnancy appeared to play no part in testicular stimulation. By substituting the immature white rat for the rabbit, Daily, in 1934, was not able to demonstrate the stimulating action of the urine of pregnant women on the process of spermatogenesis, as read by the appearance of sperm heads in the tubules.

Our interest in the report of Dorn and Sugarman needs no comment. Wishing to gain familiarity with their methods and hoping that the utilization of this test would aid in solving the cauled secret of sex before birth, the following experiments were undertaken.

METHODS

Male rabbits of known age and weight served as test animals. Note was made of the position of the testes with reference to their degree of descent. Urine, usually 10 c.c. in amount, coming from women in the latter months of pregnancy, was injected into the marginal ear veins. After forty-eight hours, or as otherwise specified in Table I, one testis was removed. In a few instances the second testis was also subsequently removed. The extirpated testis was carefully examined in the gross for evidence of enlargement, congestion, or engorgement of the surface vessels. The midportion of the testis was fixed in Zenker's solution, mounted in paraffin, sectioned at a thickness of 7 microns, and stained with hematoxylin and eosin. In the microscopic study, attention was directed to the degree of vascularity and cellular proliferation of the tubules. The stage of spermatogenesis, indicated by the formation of spermatogonia, spermatocytes, spermatids, and spermatozoa, was also noted. Preliminary observations impressed us with our inability to positively distinguish any appreciable or constant difference in the external appearance of the testes as the result of the injections of urine from women bearing male or female children. These conclusions were sometimes reached in the face of actual knowledge of the sex of the child, since the injected urine had been frequently furnished by women admitted to the hospital just prior to delivery. In every case, to evaluate properly the results of microscopic examination, sections of testes of healthy litter mates of similar size and stage of testicular descent, and which had been kept under the same environmental conditions were used for control. After having made a prediction of sex on the basis of the microscopic picture, using the criteria established by Dorn and Sugarman, this diagnosis was compared with the verified diagnosis. This served as a check on our observations and inferences. Finally, and without knowledge of the child's sex, the entire collection of slides was reexamined, and in this presentation, the criterion for the prediction of sex lay in the interpretation of the final microscopic examination of the testis. If on comparison with the control, the experimental section showed unmistakable evidence of accelerated spermatogenesis, the prediction of a female child was made. If, however, no appreciable change was apparent, a male child was foretold.

OBSERVATIONS

After numerous observations, we were able to estimate the approximate age of the rabbit and the degree of descent of the testis by the microscopic appearance of the section. The immature testis is small and the individual tubules are lined only by one or two thin layers of cells. The more mature testis is much larger and in its tubules are seen deep layers of proliferating cells ranging from spermatogonia to spermatids and spermatozoa. One must, however, stress the existence of variations in degree of development of the different tubules even within one given section, particularly in those sections showing beginning spermatogenesis. In these cases we learned the hazard of venturing an opinion as to the exact stage of development of the testis on the basis of appearance of a single microscopic field. Here and there one may see small tubules containing only a single layer of cells at their peripheries. Elsewhere other tubules in the same section may show active proliferation with formation of spermatocytes and spermatids. The entire cross-section of the testis rather than any one microscopic field must be compared with the control section before reaching a conclusion as to any stimulating effect attributed to the injection.

The findings of our study are summarized in Table I. Forty-three tests are reported. There was no exclusion of cases except two instances in which it was not

TABLE I. INJECTION OF URINE FROM PREGNANT WOMEN INTO MALE RABBITS, WITH INTERPRETATION OF RESULTS

	TEST	RABBIT		POSITION OF TESTIS	URINE INJECTED C.C.	INTERVAL BETWEEN INJ. AND EXAM. HOURS	SEX OF CHILD	
		AGE WK.	WT. GM.				MALE	FEMALE
							PREDICTION	PREDICTION
A	1	11	1350	Canal	10	48	Correct	Correct
	2	14	1020	Canal	10	48	Incorrect	
	3	16	1700	Scrotum	10	48		
B	4	9	810	Canal	15	24 & 48	Incorrect	Incorrect Incorrect Incorrect Incorrect
	5	11	780	Canal	10	96	Correct	
	6	11	1390	Canal	10	48		
	7	11½	1600	Canal	10	48	Incorrect	
	8	11½	1700	Canal	5	48		
	9	16	1700	Scrotum	10	48	Correct	
	10	14	2040	Scrotum	10	48		
	11	16½	2160	Scrotum	10	48		
	12	7	1100	Canal	10	48	Correct Correct Correct Correct ‡	
	13	7	1210	Canal	10	48		
	14	11	890	Canal	10	72		
15	8	990	Canal	10	50 & 264			
C	16	8	1350	Canal	10	48	Correct Incorrect Correct Correct Correct Correct Correct Correct Correct	
	17	11½	1620	Canal	10	48		
	18	11½	1650	Scrotum	10	48		
	19	12	1500	Canal	10	48		
	20	15	1370	Scrotum	10	48		
	21	16	2540	Scrotum	10	48		
	22	12½	2180	Scrotum	10	48		
	23	16½	2470	Scrotum	10	48		
								Correct

TABLE I.—CONT'D

TEST	RABBIT AGE WK.	WT. GM.	POSITION OF TESTIS	URINE INJECTED C.C.	INTERVAL BETWEEN INJ. AND EXAM. HOURS	SEX OF CHILD	
						MALE PREDICTION	FEMALE PREDICTION
24	7	1100	Canal	10	48	Correct	Correct
25	8	680	Canal	10	48	Correct	
26	8	820	Canal	10	48	Correct	
27	8	900	Canal	10	48	Correct	
28	8	1100	Canal	10	48	Correct	Incorrect Incorrect
29	8	1100	Canal	10	50	Correct	
30	9	800	Canal	15	24 & 48		
31	9	945	Canal	10	48		
32	9	940	Canal	10	48	Correct	Incorrect† Incorrect Incorrect Incorrect
33	9	990	Canal	10	48		
34	9	1140	Canal	10	48		
35	9	1300	Canal	10	48		
36	10	990	Canal	19	24 & 48		Correct
37	10	1400	Canal	10	48	Correct	
38	10	1510	Canal	15	24 & 48		
39	11	880	Canal	10	96		
40	11	1400	Canal	10	48	Correct	Incorrect
41	11	1590	Canal	10	48	Correct	
42	11½	1600	Canal	10	48		
43	12½	1320	Scrotum	10	48	Correct	

*Anencephalic monster.

†Female twins.

‡Male twins.

possible to learn the sex of the child because the patient subsequently failed to return to the clinic. It will be noted that most of the rabbits were in the stage of development recommended by Dorn and Sugarman, viz, they were nine to twelve weeks of age and their testes were situated in the canals. Younger and older age groups are also represented. On inspection of the table, it is apparent that one cannot group the animals according to age and directly relate such grouping to weight and position of the testes. In Group A, using rabbits of different ages and weights but with testes in a comparable position, one correct and one incorrect diagnosis of sex was made with urine of two women carrying male children in the fifth month of pregnancy. In Test 3 the testes had already reached the scrotum, but there was evidence of advanced spermatogenesis, hence the correct prediction of a female child. In the group of rabbits (Group B in Table I) receiving injections of urine from women in the seventh month of pregnancy, the correct prediction of sex was made in one of five tests in those cases in which the testes were in the canals. In those cases in which the testes already were in the scrotum, one correct and two incorrect predictions were made. Twelve cases are represented in Group C. Urine from women in the eighth month of pregnancy was injected. In only one case, Test 18, of the male pregnancies was there evidence of increased spermatogenesis on comparison with the control. Here the testes had already reached the scrotum, but the increased spermatogenesis caused us to make the incorrect diagnosis of a female child. The sex of a set of identical twins was correctly foretold. The sex of a female anencephalic monster was wrongly predicted. Urine from two women bearing female children was injected into rabbits whose testes had already reached the scrotum (Tests 22 and 23). In the former test there was no increased spermatogenesis, but in the latter test increased cellular proliferation led to the correct diagnosis of sex. In Group D 20 tests were performed on urine from women in the ninth month of pregnancy, most of the specimens of urine having been collected after the patients had been admitted to the hospital shortly before delivery. Tests 29 and 32 were on the urine of the same woman, different rabbits however being used. In each case the sex of the child was correctly predicted. In another duplicate series, Tests 36 and 38, respectively, the spermatogenic response was positive in one case and negative in the other. Of the 11 "male" specimens, 1 showed a false positive reaction. Of the 9 "female" specimens, 2 were associated with increased spermatogenesis, whereas the remaining 7, including a set of identical female twins, showed no appreciable change. Summarizing the various groups, it is noted that 5 out of the 26 specimens of urine of male-bearing gravida gave false positive reactions. Thirteen out of 17 specimens of urine from female-bearing gravida gave false negative responses.

COMMENT

Our series is admittedly too small for the basis of any but tentative conclusions. We must assert in the light of our present knowledge the jeopardy of formulating opinions as to the specific effect of the injection of the urine of pregnancy on the testis. The question of dosage, the interval between the injection and time of examination, and the variations in degree of response are all important matters to be solved. Strict accuracy in reading the end-point is difficult, and different observers might find reasons for disagreement. The suitability even of a litter mate as a control has not been established. One observation, however, appears deserving of mention. Of 26 rabbits which received injections

of urine from women pregnant with male children, 5 (19.2 per cent) showed increased proliferation of the germinal epithelium in the seminiferous tubules. Of the 17 rabbits which received urine from women carrying female children, 4 (23.5 per cent) showed similar accelerated spermatogenesis. Just what significance this observation may have, we are not prepared to state. More study will be required to clarify this point and to establish a causal relationship between the injection of any particular constituent of the urine with any particular response of the testis. We were, however, unable to correlate the spermatogenic manifestation with the sex of the unborn child. In this respect our findings correspond to those of Curphey and Romer.

SUMMARY

Urine from women in the latter months of pregnancy was injected into pubescent male rabbits whose testes were subsequently examined for evidence of spermatogenesis and compared with the testes of litter mate controls.

Testes of 9 of the 43 rabbits injected showed evidence of accelerated spermatogenesis.

These 9 cases were almost equally divided (19.2 per cent and 23.5 per cent) between the animals which had been injected with urine from male-bearing and female-bearing women, respectively.

We were unable to correlate these changes with the sex of the unborn child.

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- v. Fekete, A.: *Premenstrual Elevation of Temperature*, *Monatschr. f. Geburtsh. u. Gynäk.* 99: 29, 1935.

The investigations of v. Fekete have revealed that even in completely healthy women there is a slight premenstrual elevation of temperature which subsides when the woman lies down. There is a slight but definite rise in temperature during the few days before the menstrual flow begins and also during the early months of pregnancy. Frequently these slight fevers are accompanied by uncomfortable sensations such as restlessness, a tired feeling, drowsiness, and general malaise. In such cases if no pathologic condition can be found to account for the fever, we may assume that the elevation is due to an increase in the function of the anterior pituitary gland. This disturbance in turn is caused by a relative insufficiency in the amount of folliculin. When the slight fever is associated with disagreeable symptoms, Fekete recommends the administration of repeated doses of estrogenic substance.

J. P. GREENHILL.

PREGNANCY COMPLICATING CARDIAC DISEASE

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THIS paper is advisedly entitled "Pregnancy Complicating Cardiac Disease" because we wish to emphasize the cardiac status rather than the pregnancy. We should look upon these women as cardiac patients who have to bear the burden of a pregnancy, rather than pregnant women who have cardiac disease. This point of view will stress the importance of treating the cardiac disease first and the pregnancy afterward. A review of the literature of the past ten years shows a definite trend for closer cooperation between the cardiologist and the obstetrician, with the result that the pregnant cardiac patient is today getting better and more intelligent care than she did in the past. Most good maternity hospitals either have a cardiologist attached to their prenatal clinic, or the patient is referred from the prenatal to the cardiac clinic as soon as the heart lesion is discovered, and for the rest of her pregnancy she is watched and studied by both.

From 1924 to 1934 there were 22,100 women delivered at our hospital. Of these there were 205 with definite cardiac disease who were three or more months pregnant. This study does not include some twenty-five patients who had a therapeutic abortion done for cardiac disease in the early weeks of pregnancy. Most of the ward cases in this study were referred from the prenatal to the cardiac clinic as soon as the heart lesion was discovered. They continued to attend both clinics at frequent intervals and when admitted to the hospital for observation or in labor, they were frequently cared for by both the obstetrician and the cardiologist. Many of the private patients who showed evidence of cardiac distress while in the hospital were also seen by a cardiologist.

Most of our patients had a definite history of chorea or rheumatic fever. A few gave a history of a preceding pneumonia. One was due to syphilis (aortitis) and one was a congenital cardiac (pulmonary stenosis). The ages varied from nineteen to forty years. There were 111 primiparas and 94 multiparas. Of 205 cases, 85 had mitral stenosis alone, 90 had a double mitral lesion, 12 had a double mitral and an aortic lesion, 10 had mitral insufficiency, 1 had mitral stenosis and aortic insufficiency, 1 had mitral and aortic insufficiency, 4 had chronic myocarditis, one had congenital pulmonary stenosis, and one had syphilitic aortitis. Thus 91.7 per cent had mitral stenosis, either alone or combined with aortic disease. It is generally stated that about 90 per cent of pregnant cardiac patients have mitral stenosis.

Frequent references are made in the literature to the fact that cardiac patients often go into labor prematurely, have fairly short labors, and give birth to small babies. In our series, 34 or 16.3 per cent went into premature labor. The average weight of the babies was 6 pounds 12 ounces, a few ounces less than normal. The average duration of labor in 82 primiparas was 20.5 hours, considerably longer than normal. This is explained by the fact that there were 18 primiparas who had labors from twenty-four to seventy-two hours. The average duration of labor in 63 multiparas was 8.3 hours, a normal figure.

In classifying our pregnant cardiac patients we used the groupings advocated by the New York Heart Association and Dr. H. E. B. Pardee. We realize that the division of cases into Classes I, II A, II B, and III, is more or less arbitrary and has its limitations, yet we found it very helpful in studying the results obtained in each group. Class I consists of cases with perfect compensation, Class II A of those with fairly good compensation, II B cases are moderately decompensated, while those in Group III are badly decompensated.

The management of the pregnant cardiac patient consisted in limiting her activities in selected cases, rest in bed when necessary, the frequent use of mild sedatives, and admission to the hospital on the first signs or symptoms of cardiac embarrassment. About 30 per cent of our patients showed some signs of cardiac decompensation during pregnancy. Most of them belonged to Groups II B and III and a few to II A. Quite a number of patients were hospitalized for rest and study or for treatment for several weeks before the onset of labor or before the pregnancy was interrupted. These patients must have their cardiac condition treated as if no pregnancy existed. If the pregnancy is to be terminated, the heart is allowed to become well compensated before anything is done. Corwin, Herriek, Valentine, and Wilson have laid down the formula: "Cardiac decompensation plus forcible delivery equals death." Generally speaking, this is quite correct. These authors further state: "No attempt should be made to induce labor in a badly decompensated heart. Without delivery, the patient may die; with forcible delivery, she will almost surely perish."

Of those patients admitted in labor, the majority were given one or more doses of morphine or morphine and scopolamine as soon as possible, and the second stage was shortened by the frequent use of forceps. There were a good many patients belonging to Groups II B and III, who either had a rapid pulse and increased respirations or actually broke their compensation during the labor or immediately after delivery. During labor, the pulse and respirations are the most valuable guides we have as to the way the myocardium is behaving, because an increase in these is usually the forerunner of heart failure. While a great many of

the forceps were applied prophylactically, some were done because of an increase in pulse and respirations.

METHOD OF DELIVERY:

Spontaneous	65
Forceps	93
Version and extraction	6
Breech extraction	4
Abdominal hysterotomy and sterilization	4
Cesarean section without sterilization	8
Cesarean section with sterilization	22
Died undelivered	3
Induction by rupturing membranes	2
Induction with bag	1

With the exception of a few that were made under local infiltration, almost all of the vaginal deliveries were made under open drop ether anesthesia.

The cases handled by the abdominal route were 34 in number. Four patients had an abdominal hysterotomy and sterilization (1 at three months, 3 at four to four and one-half months) while 30 had a classical section done between the seventh and ninth months of pregnancy. Of the 30 sections, 22 patients were sterilized either by some form of tubal ligation or excision of the cornual ends of the tubes. There was one post-operative death due to a bronchopneumonia on the twenty-second day. The maternal mortality for the 34 cases was 2.9 per cent. Half of the 34 cases, or 50 per cent, had a temperature for an average of eight days. Five had wound infections, 4 had upper respiratory infections, 2 had pelvic peritonitis, 3 had phlebitis, and 2 had endometritis with foul lochia.

As regards cesarean section in pregnant cardiac patients, we feel rather strongly that it should be performed more frequently than at present because abdominal delivery under local infiltration will put the least strain on the myocardium of a certain group of cases. To be specific:

a. Cesarean section and sterilization should be done in patients who have had one or more breaks in compensation; also in patients showing evidence of myocardial damage or a severe aortic lesion, regardless into what group the case falls.

b. Cesarean section without sterilization should be done for cardiac patients who have either a borderline or truly contracted pelvis, a progressive toxemia, and for those patients who make no progress after ten to twelve hours of good labor.

In our group of 34 abdominal deliveries, 5 had a contracted pelvis, 2 had preeclampsia, 1 had no progress after thirty hours of labor, and several had electrocardiographic evidence of myocardial damage, although fairly well compensated. Four belonged to Group I, 12 to Group II A, 15 to Group II B, and 3 to Group III. Twenty were done under ether and 14 under local infiltration preceded by morphine, either

alone or with scopolamine. We believe that local anesthesia preceded by morphine and scopolamine is the ideal anesthetic for pregnant cardiac patients to be delivered abdominally, although Hamilton and Kellogg express a distinct preference for ether because they believe it to be safer, quicker, and nonexciting. About half of the patients who were sectioned were hospitalized for a variable period of time prior to operation, either for rest or for treatment. It is a mistake to operate upon a patient with a decompensated heart. This cannot be overemphasized. We also believe it inadvisable to wait for viability in patients who have been badly decompensated.

We found it convenient to divide our cases into the groups referred to previously, and in so doing, we were able to study and compare the results obtained in each group. Table I shows at a glance that as we proceed from one group to the next, the number of cardiac failures during or after labor and the number of deaths increases rather markedly.

TABLE I

GROUP	NO. OF CASES	RAPID PULSE DURING LABOR OR P. P.	FAILURE DURING LABOR OR IMMEDIATELY P. P.	DEATHS	PER CENT	CAUSE OF DEATH
I Well compensated	129	3	—	1	0.73	Subacute bact. endocarditis twenty-second day
II A Fairly well compensated	29	4	4	0	0.0	—
II B Moderately decompensated	29	—	11	4	13.7	(1) Pulmonary embolus, thirteenth day (1) Bronchopneumonia, twenty-second day (1) Subacute bact. endocarditis, eighteenth day (1) Heart failure, tenth day
III Badly decompensated	18	—	16	5	27.7	(3) Heart failure, undelivered (1) Heart failure, sixth day (1) Heart failure, tenth day
Totals	205			10	4.87	

Thus of 205 patients, 10 died, giving a maternal mortality of 4.87 per cent. In the literature, the mortality varies from 5 per cent to 10 per cent but is more often nearer 5 per cent. Reid, in a statistical analysis of the literature on pregnant cardiac patients, mentions 830

reported cases with a mortality of 5.1 per cent. From Table I it is apparent that the greatest trouble is encountered in Groups II B and III. These groups are responsible for 90 per cent of the failures during labor and also for 90 per cent of the deaths. This table illustrates the value of the groupings I, II A, II B, III from the point of view of prognosis.

Of the three patients who died undelivered, one was an ambulance patient who had never had prenatal care; patient was admitted in extremis and died in twelve hours. The other two were private patients admitted in acute decompensation, and in spite of very vigorous treatment, one died on the third day and the other on the fifth day after admission.

Twenty-two of our patients came back to the hospital either with another pregnancy or for medical care of their cardiac condition. The study of the records of this small group of cases is very instructive. These patients were seen from one to six years after a previous delivery. Of 11 patients who were originally in Group I, 3 were worse. Of 7 in Group II A, 1 died of heart failure within two years of her delivery, and 5 others were distinctly worse. Of 2 cases originally in Group II B, 1 was unchanged, while the other died of heart failure eighteen months after delivery. Thus, of 22 cases on which we had a follow-up, 3 patients were dead in two years, 8 were worse, and 11 unchanged as far as the cardiac status was concerned.

Scott and Henderson from a study of 56 autopsies of rheumatic heart disease decided that there was no conclusive evidence that pregnancy shortens the life of the patient suffering from rheumatic heart disease. Daly and Strouse feel that there is no appreciable difference at the end of several years between those cardiacs who have gone through a pregnancy and those who have not. However, the fact that a certain heart has stood one pregnancy well is no proof that it will stand the strain of another pregnancy. Our own few cases that came back seem to indicate quite the contrary, although we must be careful in drawing conclusions from such a small group.

CONCLUSIONS

1. The cardiac pregnant woman will get better care as a result of the combined efforts of the cardiologist and the obstetrician.
2. In determining whether a given heart will stand the strain of pregnancy, labor, and delivery, more attention should be paid to the cardiac reserve and less to the valvular lesion.
3. Contrary to the general impression that cardiac patients have short labors, eighty-two of our primiparas had an average labor of 20.5 hours.
4. The management during pregnancy of the cardiac who is allowed to continue her pregnancy must constantly aim either to maintain or build up her cardiac reserve. This is best accomplished by proper balancing of rest and work.

5. During labor the pregnant cardiac patient should be given sufficient rest and analgesia with morphine and scopolamine or with one of the barbiturates.

6. The pulse and respirations are the best guides as to the behavior of the heart during labor.

7. The second stage with its severe strain on the myocardium should be shortened as frequently as possible, especially if there is an increase in pulse and respirations.

8. If labor threatens to be prolonged, if progressive toxemia is present, or if there is any degree of disproportion, the case is best handled by cesarean section under local infiltration.

9. The pregnant cardiac patient who has had a break in compensation should be hospitalized and treated, and after the heart has become well compensated, the pregnancy should be terminated by cesarean section and sterilization under local anesthesia. This procedure should also be done for patients with a severe aortic lesion and those showing definite evidence of myocardial damage.

10. While there is no conclusive evidence that pregnancy shortens the life of the cardiac patient, yet the fact that one pregnancy does no harm is no proof that another pregnancy will do no harm. In fact, some of our patients who came back to be delivered again showed the reverse to be true.

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1325 UNION STREET

Guyot, J., Courriades, H., and Rocher, C.: *Metrorrhagia in the Menopause*, Bull. Soc. d'obst. et de gynéc. 23: 717, 1934.

Recent statistics have shown that 60 per cent of the cases of metrorrhagia during the menopause require no surgical treatment because the etiology is a benign modification of the uterine mucosa. The authors collected twenty-five cases of metrorrhagia among women in the change of life and found cancer of the body of the uterus in 18 per cent, cancer of the cervix in 9 per cent, fibroids in 18 per cent, polyps in 14 per cent, and hyperplasia in 50 per cent. These authors maintain that exploratory curettement permits a more definite diagnosis than hystero-graphy with lipiodol or intrauterine exploration with a hysteroscope. The authors have never seen a curettement fail to discover the lesion. Dissemination of carcinomatous cells with curettement is extremely rare.

J. P. GREENHILL.

THE INJECTION OF VARICOSE VEINS DURING PREGNANCY*

A PRELIMINARY REPORT

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THE injection method of treatment of varicose veins dates back to the invention of the hypodermic syringe in 1851. Pravas and Chasaignac (1853) injected ferric chloride to coagulate the blood. Deranges in 1855 advocated iodotannic solution. These, together with many other solutions, were tried and found to be so irritating that they were abandoned. Chiefly due to Linser, 1911, and Secord and Nabl, sodium salicylate and glucose were tried and found to give good results. Since 1921 many thousands of cases have been reported with good results with glucose, dextrose, quinine urethan, sodium chloride, sodium salicylate, and sodium morrhuate.

Of the many thousands of cases reported the most common type of varicose veins, namely that of pregnancy, was conspicuous by its absence, or it was stated empirically that pregnancy was a contra-indication. This attitude is further reflected by DeLee¹ when he states the dangers of varicosities of pregnancy as ulceration, phlebitis, emboli, and rupture with fatal hemorrhage, then adds under treatment, "Little can be done to cure the bad cases of varicosities during pregnancy, but I have helped several cases by the administration of calcium." Much the same attitude is expressed by Williams² who states, "Active treatment is useless in vulval varices, but the danger of their rupture at the time of labor should be borne in mind."

De Takats³ states, "Venous pressure in the lower extremities rises with the advance of pregnancy. Existing varicose veins are aggravated. They do not recede after childbirth, but get progressively worse with each pregnancy. The question arises whether it is advisable to treat the veins during pregnancy or whether it is better to wait until after childbirth. Based on a small experience with pregnant women (six cases), we found that the injection treatment gave them subjective relief, and if the main saphenous trunk was obliterated or ligated, the progress of the disease could be stopped. This, of course, is true only of the true varicose veins. If the deep circulation is obstructed, and if the coexisting lymphatic block produced edema, the injection treatment is obviously not indicated and will not influence a postpartum phlegmasia. This important field, pregnancy and varicose veins, needs further investigation and study."

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Hawk⁴ states, "Pregnancy when complicated by varicose veins is a decided indication for injection. Great relief is afforded these women and the procedure may be carried out up to the sixth or seventh month safely. Quinine solutions should not be used."

McPheeters⁵ published a report based on the treatment of varicose veins in 46 otherwise normal pregnancies with the following conclusions:

1. "Often a pregnant woman is made an invalid by the pain and disability occasioned by the occurrence of varicose veins and their complications.
2. "In the past, the treatment has been only symptomatic and temporary.
3. "We should no longer accept the opinion of many men that women must have pain and discomfort during pregnancy unless the causative factors cannot be removed.
4. "Injection of varicose veins during pregnancy lessens the tendency to thrombophlebitis after delivery, since the blood is more or less stagnant in a varix.
5. "It is perfectly safe to inject varicose veins during pregnancy, and by so doing we can relieve the woman of her pain and discomfort in the course of one or two weeks."

Kilbourne⁶ in a discussion of varicose veins of pregnancy gives no personal experience with the injection of varices during pregnancy, but in commenting on McPheeters' report states, "If a pregnant patient is in serious pain or discomfort, I see no objection to allowing relief by the simple expedient of injecting veins; as to the question of preventing milk leg by previous varicose vein injection, I know by clinical experience that varicose veins do develop phlebitis with a frequency not found in normal veins, however, phlegmasia alba dolens most often begins in the deep veins of the legs and later involves the superficial veins. General treatment of varicose veins of pregnancy as a prophylactic against phlebitis would not be advised. In the majority of light cases it is preferable to wait until after delivery and see if the varicose veins will not retrogress spontaneously; however, the treatment is indicated in patients with serious distress during the fourth to the seventh month of pregnancy."

These few concessions that varicose veins of pregnancy can be injected mark a fundamental change. If we study the history of any medical or surgical advancement, we find that the pregnant woman is the last to receive its benefits. For years no one dared do an appendectomy on a pregnant woman. More recently the same was true of thyroidectomy, yet no one now hesitates when these procedures are indicated. The objections to treating varicose veins of pregnancy are long standing and deeply ingrained into the public and the profession. Ambrose Pare⁷ wrote of them in 1579. "Women with child are commonly troubled with them by reason of the heaping together of their suppressed menstrual evacuation. It is best not to meddle with such as are inveterate for such being cured there is to be feared a reflux of the melancholy blood to the noble parts whence there may be danger of malign ulcer, a cancer, madness or suffocation." Pigeaux warned of a case of abortion in a cook following the bandaging of varicose veins. The same deep-seated objections to treatment during pregnancy are seen today when week after week we see in the office patients with large painful varicose veins who refuse treatment be-

cause of their own fear of being treated until after delivery, or because they have previously and usually repeatedly been told by physicians that they should wait until after delivery for treatment. Further evidence of this opposition to treatment is seen in the fact that we were able to treat only twenty-four patients during the past nineteen months, while we had 503 deliveries during that time. This is rather more impressive when we consider that DeLee⁸ states, "Nearly everyone has at least one or more phlebectasias. In 20 per cent of the cases the varicosities are marked."

It should be mentioned here in partial explanation of the small percentage of treated cases that in no case was injection treatment urged upon any patient. We wanted an honest opinion from the patient as to the benefit, if any, she derived from the treatment, and we did not feel that we would get an unbiased opinion if the patient already had a definite fear or opposition to treatment during pregnancy, and especially if her objections were founded on advice from her family physician. It was chiefly because of this combined opposition of patients and doctors that it was decided to give this preliminary report much earlier than was originally intended.

The purpose of this work was twofold:

1. To prove the injections of varicose veins of pregnancy a safe procedure at any stage of pregnancy, for any size varix at any location.
2. To try and arrive at some definite conclusion as to which veins should be injected and which left alone.

To do this we have injected every case of varicose veins of pregnancy which would submit to treatment. We have set no limitations on the location or size of the varix. We have set no limitations on the period of the pregnancy, except that no injections were done in the last two weeks of pregnancy, and this limitation was set because we wanted all patients ambulatory during treatment. The contraindications for varicose veins of nonpregnant patients have been observed. Sodium morrhuate was used exclusively. We submit twenty-four cases. Of these, twenty-two are delivered. The site of injection ranges from the ankle to Poupart's ligament and the vulva. The size of the veins treated varies from superficial, unimportant varices (three cases) to varicose veins so extensive as to force the patient to be in bed. One patient came to the office via ambulance until after injections were started. The number of injections varied from one to seven. The average injection was 3 c. c. The ages of the patients varied from eighteen to thirty-seven years. The earliest stage of pregnancy when treatment began was four months, the latest seven and one-half months. Several were treated to within fourteen days of expected delivery. There were three primiparas in the series.

RESULTS

We had one local reaction with no untoward results for mother or baby. No treated patient failed to be relieved. No treated patient had any postpartum complication with the circulatory system. No treated patient was hospitalized longer than the untreated patient. Each patient on completion of the treatment was asked this question, "If, now that you have had the treatment and know what it is like, you had the choice of keeping the veins or having the treatment, which would you choose?" Two chose the veins, the remainder the treatment.

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208 JEFFERSON AVENUE

MOTILITY IN THE TRANSPLANTED, DENERVATED UTERUS*

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THE purpose of the present investigation is to demonstrate the relationship between the innervation (extrinsic and intrinsic) of the rabbit's uterus and the myometrial action of estrin and progesterin. Ample evidence exists to show that estrin is specifically necessary for initiation of coordinated rhythmic motility and for the sustaining of such activity in the normal uterus.¹⁻⁶ It is also known that progesterin, on the other hand, exerts a very strong inhibiting effect on rhythmic, estral contractions.⁶⁻¹⁵ That portions or all of the excised uterus will contract rhythmically and under suitable circumstances even simulate parturition has, of course, long been known. It has only recently been shown, however, that spontaneous rhythmic motility is observed in vitro only when the uterus is under the influence of estrin at the time it is removed from the body.^{3, 4} The fact that the excised, quiescent uterus cannot be made to contract rhythmically by treatment with estrin even though large quantities be added to the perfusion bath is most important.

The present experiments have been done to ascertain the effects of estrin and progesterin on the transplanted denervated uterus.

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EXPERIMENTAL

The plan of the experiments was a simple one. One uterine horn was transplanted, as described below, from its normal site to a position on the anterior abdominal wall, there taking up a new blood supply. In the process of completing this transposition, all the original nerves to the uterus were severed. Inasmuch as sufficient time was allowed for complete degeneration of the nerve paths and since it has been shown that there is no extensive intrinsic uterine motor nerve plexus,¹⁶ it was possible for us to investigate in the essentially denervated uterus two things: first, the degree of activity associated with various sexual states, viz., oophorectomy, estrus, and pseudopregnancy; and second, the effect of replacement therapy with estrin.

STEPS IN THE OPERATION

First Stage (Fig. 1).—A mature female rabbit, weighing approximately 3½ kg. was anesthetized with ether. A longitudinal incision was made to the right of the

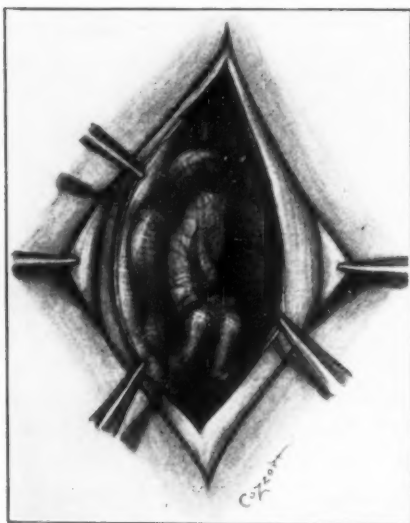


Fig. 1.—Operation, first stage.

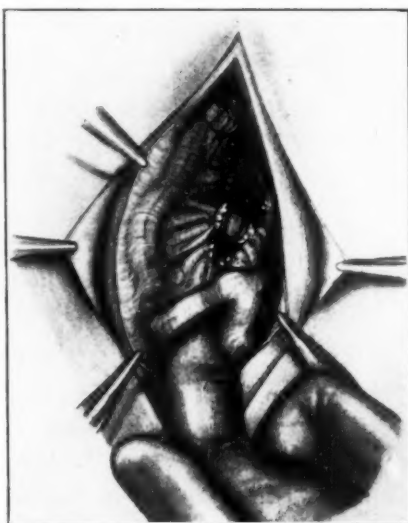


Fig. 2.—Operation, second stage.

midline, starting about three centimeters above the symphysis and extending cephalad a distance of six to eight centimeters. The right uterine cornu was brought up into the wound, the tubal end clamped, transected, and ligated, the ligature including the ovarian artery and whatever veins accompany it. The free border of the uterus was then scarified as was an area on the peritoneal surface of the anterior abdominal wall parallel to the original incision and about a half centimeter lateral to it. The scarified areas were approximated by means of interrupted sutures of plain catgut. These sutures penetrated half the thickness of the muscle coat of the uterus. At the conclusion of this stage there was a ventrofixation of the uterus.

Second Stage (Fig. 2).—After an interval of from one to three weeks or even longer, the second stage was undertaken. The abdomen was again opened, this time in the midline in order to avoid adhesions. The index finger of the left hand was passed over the cervical region of the uterus into the channel produced by the adhesion of this organ to the anterior abdominal wall. In this way the entire mesometrium was brought into view. This tissue was then incised and ligated with

interrupted catgut suture ligatures in such a manner as to sever the uterus from its normal surroundings except for its cervical attachment.

Third Stage (Fig. 3).—After another interval of from one to three weeks, the animal was opened for the third time. The vaginal tube was transected, care being taken to include all remaining mesometrial tissue on the right side. The left uterine cornu was then severed close to the cervix. As a result, the transplanted uterus terminated in a cuff of vagina containing two cervices. The entire organ was dependent for its nutrition on the vessels passing through the adhesions along the abdominal wall and also occasionally those to the intestines. The vaginal cuff was brought up through the incision and anchored to the skin so that the two cervices protruded. Records of motility were obtained by the method described by one of us,⁹ using pressure changes in a balloon inserted through the fistula.

In some animals at the beginning of the third stage, the transplanted uterus was

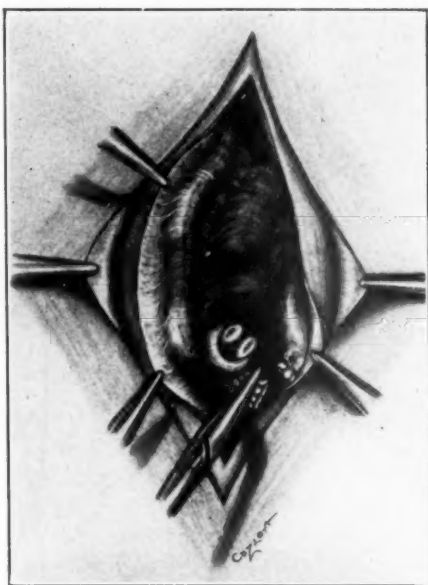


Fig. 3.—Operation, third stage.

severed from its cervix, leaving intact the vaginal canal, the two cervices, and the normal left uterus. The lowermost portion of the right uterine cornu was brought up through the abdominal wall, resulting in a transplanted, cervicectomized uterus. In addition, a fistula was sometimes made using the nontransplanted left uterus according to the method previously described.⁸ Contractions were then recorded in the same fashion as in the noncervicectomized uterus.

The above operative procedures have been previously described¹⁰ but are included for the sake of completeness.

RESULTS

The following results are based upon data obtained from seven rabbits. In order to determine whether the nerve paths had been entirely severed, the presacral nerve was stimulated in each animal just before it was killed. Data from those rabbits in which a response of the uterine transplant was elicited were rejected. Although the number of rabbits finally

used is admittedly few, the completeness of the operation and the consistency of the results give ample evidence of the activity of the denervated uterus in response to stimulation by the ovarian hormones, estrin and progestin.

The results are presented under two headings, relating to the activity of each of the hormones mentioned.

1. Rhythmic contractions of the transplanted uterus. We observed rhythmic motility under three distinct circumstances:

A. Very marked contractions occurred spontaneously in two rabbits in which the ovaries were left in situ. Such motility is present in the nontransplanted uteri when nonpregnant rabbits are in heat and is lacking when they are not in heat.² Large graafian follicles normally present when this estral motility is observed were present in these animals. Thus, it is demonstrated that the transplanted uterus is capable of exhibiting normal estral motility. The hormone specifically responsible for such motility is known to be estrin.²

B. In three animals, ovariectomy was performed and then estrin (theelin*) was injected. In one of these in which the cervix had been severed, the effect was observed twice. Four times, therefore, it was found that estrin induced rhythmic motility in a previously quiescent, transplanted uterus (Fig. 4).

C. In another rabbit, rhythmic motility followed an extended interval of inactivity during a period of pseudopregnancy (Fig. 6).

Thus it is clear that not only can rhythmic contractions be sustained in a transplanted uterus, but they can be initiated as well. Moreover, this is true whether or not the cervix is attached to the transplanted tissue.

2. Hormonal inhibition of motility in the transplanted uterus. In three animals made pseudopregnant by the injection of pregnancy urine, spontaneous motility was inhibited. It was found that at this time we were unable to induce motility (Fig. 5, A) by means of estrin. Thus, the transplant was found to be unresponsive to its normal hormonal excitant, estrin, when under the influence of progestin, furnished by the rabbit's own corpora lutea.

These results are consistent in every way with earlier observations^{8, 10} which showed that, when the nontransplanted uterus is under the influence of progestin, it is quiescent and cannot respond with rhythmic motility to estrin administration.

PROTOCOLS

Protocol 1.—Animal 573 (Fig. 4).

Nov. 17, 1934: First operative stage.

Jan. 26, 1935: Second operative stage.

Feb. 7, 1935: Third stage and ovariectomy, bilateral. Fistula of cervicectomized right uterus, transplant.

Feb. 10, 1935: Record (Fig. 4, A). No spontaneous motility in normal uterus; no record made from transplant.

*Generously furnished by Parke, Davis and Co.

- Feb. 11, 1935: Theelin, 100 rat units, intravenously.
- Feb. 12, 1935: Record (Fig. 4, *B*). Normal fistula showed moderate motility but some degree of irregularity. Cervicectomized transplant showed very slight motility. Theelin 100 rat units.
- Feb. 13, 1935: Record (Fig. 4, *C*). Normal fistula, good motility, fair regularity. Transplant, good motility and fair regularity. Theelin 100 rat units.
- Feb. 14, 1935: Record (Fig. 4, *D*). Normal fistula showed good motility and more regular contractions than Feb. 13, 1935. Transplanted fistula also showed better motility and regularity. Theelin 100 rat units.

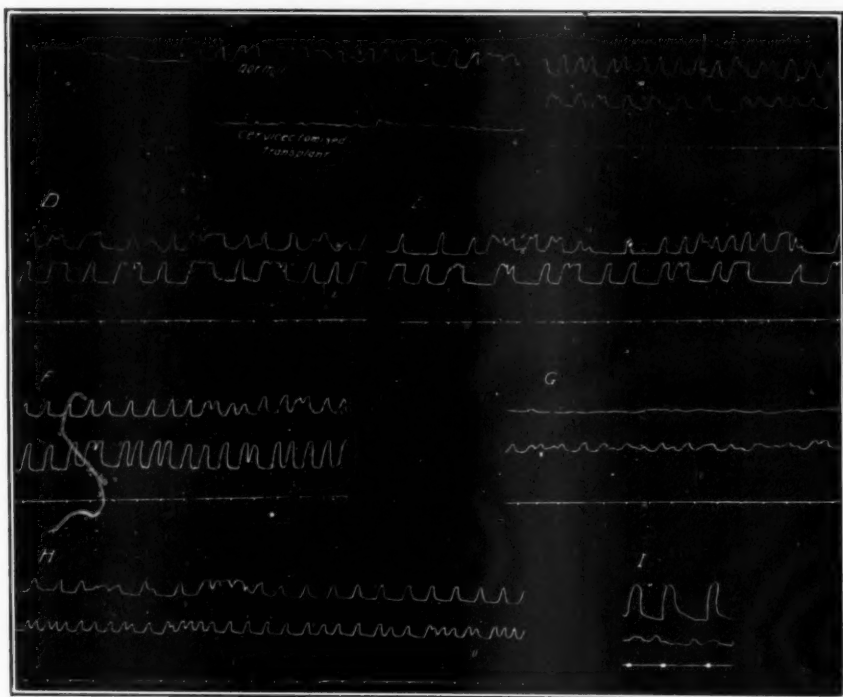


Fig. 4.—For explanation, see Protocol 1, animal 573, and text.

- Feb. 15, 1935: Record (Fig. 4, *E*). About the same as Feb. 14, 1935.
- Feb. 16, 1935: Record (Fig. 4, *F*). Rhythmicity very definite, contractions strong.
- Feb. 18, 1935: Record (Fig. 4, *G*). No theelin for four days. Normal fistula showed no contractions, transplanted fistula a few irregular small contractions. Theelin 50 rat units.
- Feb. 19, 1935: Theelin 50 rat units.
- Feb. 20, 1935: Record (Fig. 4, *H*). Contractions returning, normal uterus somewhat irregular, transplant more nearly regular.
- Record (Fig. 4, *I*). Animal anesthetized with dial, abdomen opened. Transplant in excellent condition, no infection. Presacral nerve stimulated. Responses in normal, not in transplanted uterus.

Protocol 2.—Animal K-15 (Fig. 5).

- Jan. 3, 1935: First stage, right ovariectomy.
 Jan. 17, 1935: Second stage.
 Feb. 4, 1935: Third stage.
 Feb. 6, 1935: Five cubic centimeters of urine of pregnancy.
 Feb. 11, 1935: Theelin, 150 rat units.
 Feb. 12, 1935: Record (Fig. 5, *A*). One week pseudopregnant. No motility in either the normal or transplanted fistula.
 Operation—left ovariectomy. Many large corpora lutea seen.
 Feb. 13, 1935: Theelin, 75 rat units.
 Feb. 14, 1935: Record (Fig. 5, *B*). Marked motility in both the transplanted and the normal fistulas.

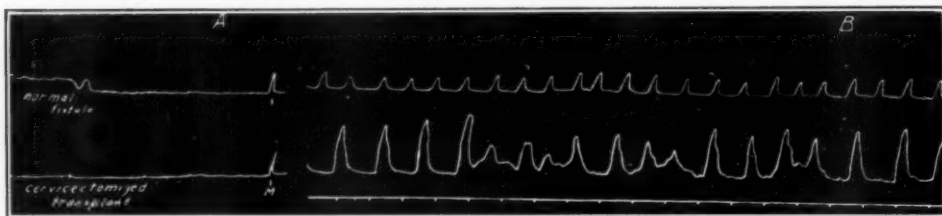


Fig. 5.—For explanation, see Protocol 2, animal K15.

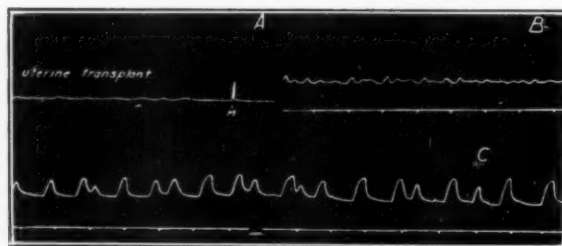


Fig. 6.—For explanation, see Protocol 3, animal K2.

Protocol 3.—Animal K-2 (Fig. 6).

- Sept. 8, 1934: First stage.
 Sept. 22, 1934: Second stage.
 Oct. 3, 1934: Urine of pregnancy, 10 c.c.
 Oct. 5, 1934: Third stage. Some sloughing of the cervix, the rest of good color. Very easy access with balloon.
 Oct. 16, 1934: Record (Fig. 6, *A*). Thirteenth day of pseudopregnancy. No motility in the transplant.
 Oct. 17, 1934: Theelin, 50 rat units.
 Oct. 18, 1934: Theelin, 150 rat units.
 Oct. 19, 1934: Record (Fig. 6, *B*). Sixteenth day of pseudopregnancy. Slight motility, irregular.
 Theelin, 50 rat units.
 Oct. 22, 1934: Record (Fig. 6, *C*). Nineteenth day of pseudopregnancy. Large contractions, rhythmic motility in transplant.

DISCUSSION

There exists in the literature ample evidence to show that uterine function is not materially modified when the nervous connections of that organ to the central nervous system are severed. Those who have transected the spinal cord,¹⁷ destroyed it¹⁷ or performed lumbar sympathectomy without subsequent interruption of conception, gestation, and parturition,¹⁸ justifiably claim that such nervous connections are probably not essential for the functioning of the uterus. Our results confirm this conclusion, as regards the estral and pseudopregnant uterus. It is a fact, however, that those who have heretofore claimed to have severed the main nerve paths to the uterus have also failed to adduce undeniable proof of the completeness of their operations. We have taken this precaution and have accepted as satisfactory only those animals in which the transplant failed to respond when the presacral nerve was stimu-

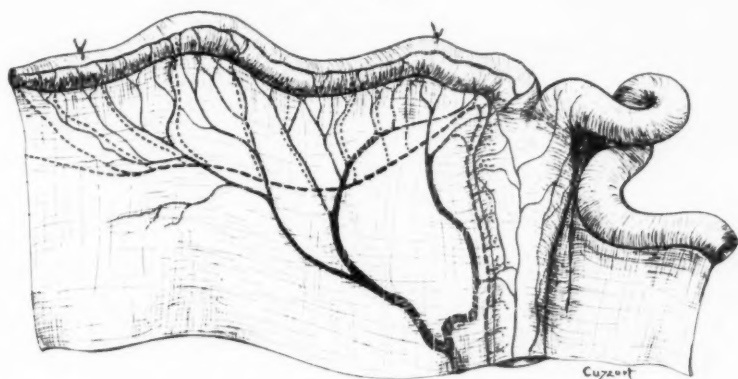


Fig. 7.—Innervation to uterus, shown in broken lines. (Reprinted from *Am. J. Physiol.* 112: 640, 1935.)

lated. The results of the present study show unmistakably, therefore, that the connection of the uterus to the central nervous system is not essential for the known action of estrin and progesterin. Yet, one may ask, to what extent do these hormones depend upon the intrinsic innervation of the uterus for their effects?

The main peripheral paths of the motor sympathetic innervation of the rabbit uterus lie in the parametrium and are distributed to each cornu locally, forming no extensive intrauterine connections¹⁶ (Fig. 7). It is also true that the cervical ganglia play no essential part in regulating the responses to the hormones studied since the cervix has been removed in some of the transplants without modification of the activity. Because, then, the uterus without the cervix is virtually devoid of nerve cells and because in the procedure of transplanting the uterus all the parametrium is severed and ample time allowed for degeneration, we are forced to the conclusion that the stimulating action of estrin on the

one hand and the inhibiting effect of progestin on the other are each mediated independently of the extrinsic and intrinsic motor sympathetic innervation.

It should be noted in passing that Langley and Anderson have shown that there are no inhibitory sympathetic fibers to the rabbit uterus and that there is no sacral autonomic innervation. While this last has been questioned, certainly the sacral autonomic innervation to the uterus is at best inappreciable.

In view of the above considerations it would appear, therefore, that the ultimate rôle of estrin and progestin activity in relation to uterine musculature must be investigated through the chemical changes that take place in the uterus itself following the administration of these hormones. But the possibility that the synergistic action of other endocrine factors may be essential for the normal effect of these hormones must not be overlooked.

CONCLUSIONS

1. Estrin maintains rhythmic contractions in the transplanted uterus.
2. Estrin also induces such contractions in the previously nonmotile transplanted uterus.
3. Progestin inhibits estral rhythmic contractions in the transplanted rabbit uterus.
4. The myometrial effects of these two hormones are essentially myogenic, the extrinsic and intrinsic innervation being nonessential.
5. Although the action of estrin is myogenic, this hormone is incapable of inducing rhythmic contractions in vitro but can do so in the transplanted uterus in vivo.

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ELECTROUTEROGRAPHY

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THE following means have been employed to study and report the contractibility of the uterus:

1. Abdominovaginal palpation of the human uterus
2. The muscle strip method in animals
3. Observation of exposed or excised animal uterus
4. Mechanical tracings of pressure variations
5. Uterosalphingography
6. Electrical methods

1. *Palpation of the Human Uterus.*—Much information on the form variations, contractions, etc., of the human uterus can be obtained from the simple procedure of bimanual palpation in trained hands.

Dickinson (*Human Sex Anatomy*) presents a thorough survey of the information to be gained from such an examination. Furrows and ridges, areas of hardenings and softenings, changes in shape, size, and position, all give evidence of the activity of the nonpregnant uterus. He says, "The uterus appears to me to develop special degrees and rhythms of contraction at the time of ovulation, . . . relative quiescence follows menstruation, then activity develops during the time both ovaries are large and tender and while one shows protrusion, and then distinctive quiescence recurs until just before menstruation."

2. *The Muscle Strip Method.*—A strip of uterine muscle is so arranged that its contractions are recorded on a kymograph by a muscle lever, giving a mechanical tracing.

With this method Blair (1922), using the white rat, showed the maximum contractions to be greater during diestrus than during estrus. Keyes (1923) using excised muscle strips of the domestic sow, demonstrated the differences in the spontaneous rate of contraction at different times in the estrus cycle. He demonstrated two types of contractions, large and small, occurring at the same time. During the period of development of the graafian follicle and shortly after its rupture, the large contractions predominate. Keyes believes that the maturing corpus luteum inhibits the large contractions and causes the short contractions to predominate.

3. *Observations on the Excised or Exposed Animal Uterus.*—The excised whole uterus when kept at body temperature in oxygenated Locke's solution may be restored to spontaneous contraction.

Seekinger (1923) studied the contractions of the tube of the sow in vitro. He states that contractions appear first about nineteen days before rupture and terminate

after the follicles have ruptured and the ova have entered the uterus. During the ripening of the follicle the contractions are short and rapid. After the ova appear in the uterus, the contractions change to a slow rhythm. Wislocki and Guttmacher (1924), studying the uterus and tubes of the sow, verified the cyclic changes observed by Seckinger. Brouha and Simmonet (1927), using the guinea pig's uterus, made periodic observations on a series of excised contracting uteri and confirmed the differences in rate and strength of contractions at different points in the estrous cycle.

Ingenious methods were devised for observing the uterus in situ in the living animal. Wijsenbeek (1922), Mikulicz-Radecki and Westman (1926) so attached the cecum to the abdominal wall in rabbits as to wall off the uterus from the other abdominal organs, and then installed a small glass window in the abdominal wall so that the uterus and tubes could be observed. Mikulicz-Radecki found the abdominal window method unsatisfactory and reverted to the muscle strip technique. Westman (1926) working on rabbits found very active muscular contractions of the tube in connection with follicular ripening. These contractions were strongest during estrus just before rupture when ripe follicles are present. He believes the corpus luteum has an inhibiting effect on the contractions.

4. Mechanical Tracings of Pressure Variations.—While the uterus is contracting, the cavity naturally undergoes variations in size. If the cavity be filled with fluid, this fluid undergoes variations in pressure. If a tube is led from this fluid to a manometer or a tambour and a lever installed, a kymographic record of these pressure changes can be made which will be a fair index of uterine contractility under conditions involving an irritant within the cavity.

The fluid in the cavity of the uterus may be lying free, in which case a cannula is introduced into the cervix to make an air-tight system. On the other hand, this fluid may be contained in a rubber bag or balloon which is introduced into the uterine cavity first and later is distended with fluid.

Two interesting early experiments of this sort are mentioned in Dickinson's *Human Sex Anatomy*. Heinricius (1889) and Aeconci (1891) introduced small rubber balloons into the uterine cavity by means of narrow silver sounds. The balloons were filled with water and the water column connected to recording manometers.

Heinricius notes three sorts of contractions: those synchronous with the pulse which he considers pulsation of a uterine artery and which are inconstant depending on impingement on or near such an artery, those which are respiratory in rhythm which also vary in clearness, and finally, those which seem clearly uterine. He gives the duration of a contraction as varying from thirty seconds to three minutes.

Aeconci also notes the presence of uterine contractions in the nonpregnant human uterus but gives the rate of contraction as seven to eight per minute.

Reynolds (1929) introduced into rabbits' uteri a tiny rubber balloon which he filled with water. This was preceded by an operation, hemisecting the vagina and creating a uterovaginal-abdominal wall fistula which gave better access to the uterus. Excellent kymographic tracings were obtained but the question arises, as in all these methods, whether artificial distention of the uterus effects or distorts contractions and gives a picture or rhythm unlike those that are spontaneous. He made no attempt to draw any exact conclusions.

Knaus (1929) used this method in extensive studies on ambulatory patients. He filled the uterine cavity with oil and depended on the conic shoulder of the salpingography cannula to keep the system air tight. The result of these studies, which depended upon the principle that pituitrin is ineffectual in causing uterine contractions in the presence of a corpus luteum, was roughly to fix the date of ovulation with special reference to the "safe period." He found normal uteri in women with twenty-eight-day cycles; spontaneous rhythmical contractions occur during the first fourteen days of the cycle and the uterus at this time responds to injections of pituitrin. Beginning at the sixteenth day, there are no more spontaneous rhythmical contractions and no response to pituitrin. The return of uterine activity does not occur until the day preceding menstruation.

Very recently Adair and Davis (1933) introduced rubber bags into the post-partum human uterus. The bags were distended with sterile water. The kymographic tracings were very clear. The effects of certain oxytocic drugs were shown.

5. *Uterosalphingography*.—A natural outcome of the x-ray picture of the uterine cavity filled with an opaque medium was the "G. I. Series" of the uterus, and the observation, under the fluoroscope, of the continuous variations in size and shape of the outline of the distended or partly distended uterine cavity.

Schultze (1929) made this the means of extensive studies of the mode of contraction of the uterus in ambulatory cases. These studies seem to show that the uterus has three functionally contracting segments, the main part of the fundus and the two horns. Both maximal contractions involving all three segments and partial contractions involving only one or two segments occur or progress from above downward. In this work the contraction of the uterus seems to have as its partial object, the emptying of the uterus of its unnatural contents. Therefore the objection arises that while the manner of contraction may be characteristic, the stimulus to contraction may be of artificial provocation.

6. *Electrical Methods*.—These are based on the familiar "action-current" of contracting muscle. As in the case of the electrocardiograph, two contacts are required to "lead off." The type of contact point varies. Some observers have used metal electrodes (usually silver), others have used physiologic or nonpolarizable electrodes. Leads have been taken in animals from points on the external surface of the exposed tube and uterus; in human beings, from the cervix, the rectum, the external abdominal wall, and even the extremities. The recording instrument has usually been some form of string galvanometer.

Work of this nature was begun about 1910. Theilhaber (1910) placed one electrode on the cervix and the other in the rectum at the height of the fundus. He obtained curves by this method which apparently were not cardiac or respiratory. They were not present in women after the menopause or in cases following hysterectomy. However, since they were not followed through the entire cycle from one period to the next, we have no way of correlating them with the behavior of the uterus at various parts of the cycle.

Veit (1912) attempted to record the uterine contraction coincident with labor pains, apparently with little success. He obtained records of contractions when he

used a lead from the feet, but when the arms were used the heart contractions obliterated all others. Blumenfeldt and Dahlman (1913) obtained records by leading directly from the puerperal uterus of laparotomized rabbits. The uterus, in this work, was abnormally stimulated. A pressure system recorded mechanical curves at the same time, and it was noticed that the electrical and mechanical oscillations were not simultaneous. Metal electrodes were used.

Greene (1928) working with nonpolarizable electrodes on the excised automatically contracting rat uterus noticed two different electrical curves, a slow, large deflection of thirty- to forty-seconds' duration and small, rapid deflections of about one hundred and twenty per minute. Myograms were taken at the same time and the electrical action currents were found to start before the mechanical contractions.

Bode (1931) obtained electrometrograms of the pregnant human uterus which he stimulated to contraction with injections of pituitary gland secretion.

A very thorough piece of work was done on the exposed uterus of the virgin rabbit *in situ* by Bun-ichi Hasama (1930), using nonpolarizable electrodes. Needle electrodes were also tried and gave similar results. He was able to show the registration of the action current of observed peristaltic muscle waves that passed through the uterus, from tubal cornu to cervix. The electrometrogram was a regular diphasic curve with the approximate rate of three to seven curves per minute. The intensity of the action current curves and the mechanical movements were not always parallel. The frequency and amplitude of the electrical curves varied in different parts of the uterus. Action currents could be obtained from the circular musculature, the amplitude of which was less but the frequency the same as the longitudinal.

A still more recent piece of work along this line was that of Vozza (1933) who ran an electrical and a mechanical pressure system in parallel. Both systems were so arranged as to register on the same strip of film. The pressure system was "lead off" from the uterine cavity through a small opening in one of the uterine cornua. The electrodes were of silver and were placed upon the ends of the isolated cornu. The rabbits in this experiment were at the beginning of pregnancy.

Vozza concludes that "there was a rather intimate relation between the mechanical contractions and the bioelectrical phenomena, but the bioelectrical changes preceded by a fraction of a second the mechanical movements." There were, however, occasional exceptions to this parallelism.

The electrical curves were of three types. The first was a slow type, made up of a series of smaller oscillations (12 to 20 to the curve), which more or less corresponded to the mechanical curve. The second type seemed rather to be stimulated by the injection of pituitrin or gynergen. The length in seconds of these different types of curves varied between ten and fifty seconds. In the third type the contractions were between 90 and 110 per minute.

The theory that the human uterus, a relatively large muscular organ, undergoes spontaneous contractions in its nongravid state led us to attempt to verify this by securing permanent tracings of these contractions, using a direct electrical "lead off" from the uterus through the electrocardiograph.

TECHNIC OF THE PRESENT INVESTIGATION

Simple electrodes that were easy and safe to apply in the human uterus were constructed (Fig. 1). The lead from the fundus is a slender curved rod of silver, two inches in length, which slips easily into the uterus. It is attached to a long, insulated wire stem, at the other end of which is an adapter for connection with the lead from

the string galvanometer. Over this wire stem, but insulated from it, slides a narrow tube of bakelite, at one end of which is a concave silver disk, the lead from the cervix. A thin wire buried in the bakelite tube connects the disk with the adapter at the other end of the tube (Fig. 2).

The cervix is exposed through a duck-billed speculum. The cervix is mechanically cleaned and tincture of iodine on an applicator applied. The electrode is introduced

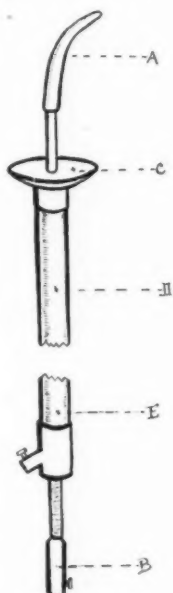


Fig. 1.

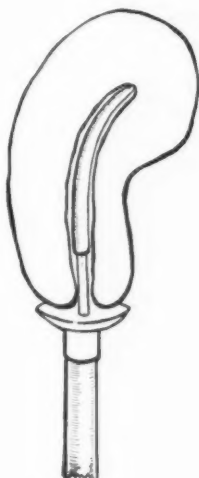


Fig. 2.

Fig. 1.—Electrode. *A*, Silver rod which enters uterine cavity; *B*, insulated wire stem from *A*, with adapter for lead from galvanometer; *C*, concave silver disk as contact with cervix; *D* and *E*, bakelite tube containing buried wire with adapter for string galvanometer.

Fig. 2.—Electrode in place in uterus.

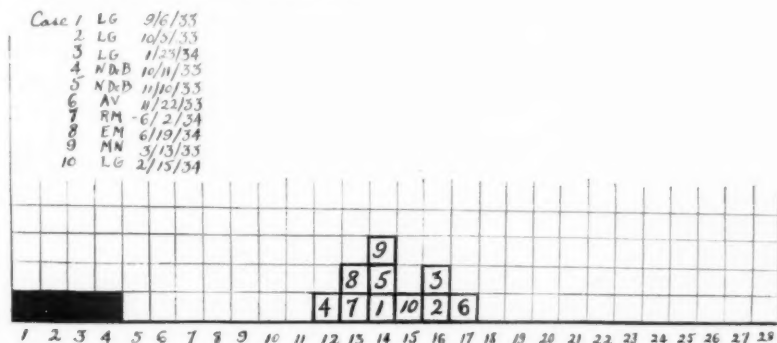


Fig. 3.—Shows what day in cycle contractions were recorded.

and the speculum removed, leaving the electrode in place. The two leads from the string galvanometer are then connected to the adapters of the electrode. Lead II of the electrocardiograph was used.

Every effort has been made to secure as many records as possible on the same patient, beginning a few days after the end of menstruation and continuing almost up to the onset of the next period.

As one follows a few women through several months in this manner, a distinct form of movement of the galvanometer string is recognized. These movements occur with a definite periodicity in the cycle (Fig. 3). The waves are irregularly rhythmic.

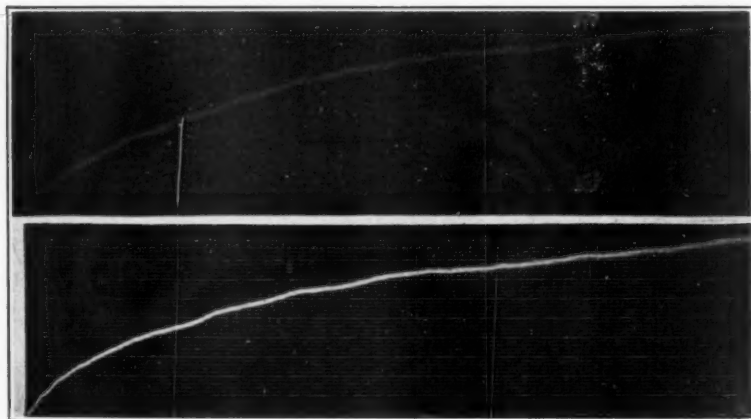


Fig. 4*.—Almost total absence of string activity. Readings taken A, eight and B, ten days postmenstrual.

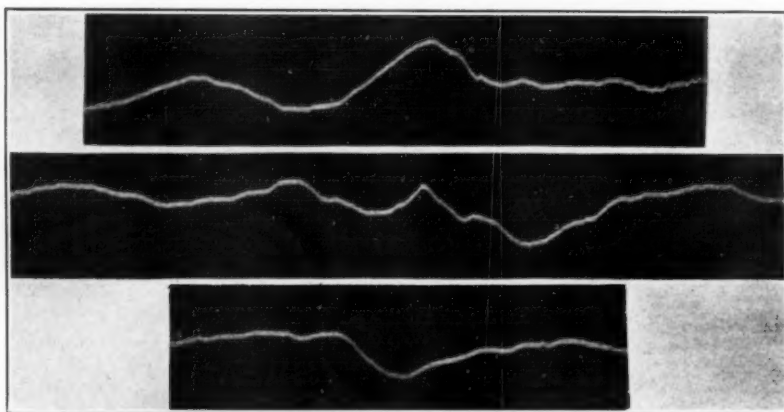


Fig. 5.—String galvanometer activity on thirteenth day postmenstrual.



Fig. 6.—Reading of string galvanometer twenty-third day postmenstrual; no activity.

They differ moderately, one from the other, in duration and intensity. The average length of the wave is about twenty seconds. This, however, varies and waves of as often as three to four seconds and as slowly recurrent as forty seconds have been re-

*Tracings shown in Figs. 4, 5, and 6 are from the same patient.

corded. When tracings are taken at frequent short intervals, every two or three days throughout the entire month, the contractions begin to appear on or about the ninth day (Fig. 4). They seem to be most marked from the twelfth to the sixteenth day (Fig. 5). They may be present, although diminished, up to the eighteenth or nineteenth day and are rarely found from the twentieth day up to the onset of menstruation (Fig. 6).

Success in demonstrating these waves depends greatly upon the introduction of the inner electrode well into the interior of the uterus and upon the elimination of interfering currents and string wandering.

In the reading of the records obtained there are a number of forms of string activity which must be recognized as artifacts and ruled out.

1. *Artifacts Due to Extraneous Disturbances.*—Slamming of doors, moving of heavy bodies, passing of elevators, and loose electrical connections, produce a series of fine "jiggling" waves which are coincident with that particular disturbance.

2. *Artifacts on the Part of the Patient.*—Strenuous movements of the legs or hips, coughing, straining, sudden very deep breathing and violent peristalsis (as from a recent cathartic), all produce marked irregular deflexions of the string. These disappear with the cessation of the activity.

3. *Pulse Wave.*—Small but definite and regular wavelets occur whose rate is exactly that of the heart. They are superimposed upon whatever other larger waves there may be. One may regard these as a transmission of the cardiac impulse. Against that, however, is the fact that frequently they are entirely absent. It is possible that these small regular wavelets may be in the nature of a "pulse jerk" occurring with uterine engorgement.

4. *Tiny Wavelets.*—Tiny "jiggling" wavelets resembling those of the extraneous causes of known origin mentioned in Group 1, occasionally occur without any perceptible cause.

5. *Wandering of the String.*—In the case of wandering of the string (a phenomenon familiar enough to electrocardiologists) the galvanometer string, when set at one edge of the recording strip, more or less rapidly drifts across the strip and off on the opposite side. It has to be brought back again. While annoying, this wandering does not completely interfere with the registration of the other forms of activity that occur, superimposed upon it. Wandering of the string is commonly attributed to secretions, grease, and impurities at the point of contact of the electrode and the tissues, these being factors which set up interfering surface current. Incidentally, it was thought that wandering of the string occurred at certain periods, the exact definiteness of which could not be determined. An interpretation of this "wandering" led to the belief that there was a more or less periodic change in the reaction of the secretions in the uterine cavity. This would have to be proved by further study.

SUMMARY OF OBSERVATIONS

Six patients were followed through a total of fifteen menstrual cycles. One hundred and three readings were taken. As many as nine records were made on one patient during one menstrual interval. The degree of thoroughness with which these cycles were investigated and the number of records made depended upon the cooperation of ambulatory clinic patients and, therefore, varied considerably. In three instances, only two readings could be obtained throughout one entire menstrual interval. While these in themselves would be utterly inconclusive, they can be

interpreted, however, when combined with observations on other menstrual cycles, on the same and other subjects, which were studied more completely.

Eleven menstrual cycles were completely studied on five patients; of these eleven, ten showed a definite increase in string activity from the ninth to the eighteenth day.

The interpretation of the origin of these waves is somewhat problematical. They seem to be of uterine origin. They are much too slow for heart or respiration. They are slow enough for smooth muscle, and there can be no question that they "led off" directly from the uterus. If they represented the muscular activity of an adjacent organ such as bladder, intestine, or colon, one would *not* expect any definite rhythmic cycle of contraction from the tenth to fifteenth day of the cycle. Repeated injections of theelin seemed irregularly to augment these waves. This, too, would argue against the activity of another organ. As these waves occur at the time supposed to be the ovulation period, the waves might be a record of tubal peristalsis. This, however, is very doubtful. Seeking shows that maximal tubal contractions occur later in the cycle.

If these periodic increases in string activity do represent increased contraction of the uterus, this will be a means, however imperfect, of recording the spontaneous contractions of nonpregnant uteri. Furthermore, as these contractions are apparently coincident with the pressure, if not life, of the developed follicle or the recently expelled ovum, this method may give indirect information regarding stages of ovulation. Theoretically one might explain the absence of contractions up to the eleventh day to a low amount of folliculin, from the eleventh to the twenty-first day ample folliculin, after the twenty-first day the inhibition of corpus luteum.

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HISTORICAL REVIEW OF A SYNDROME EMBRACING UTERO- OVARIAN ATROPHY WITH PERSISTENT LACTATION (FROMMEL'S DISEASE)

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ATROPHY of the uterus and ovaries associated with lactation is a syndrome of historical if not of current interest. Priority of description of this entity appears to have been accorded Richard Frommel¹ of Berlin as a result of his study of 28 cases published in 1882.

It is noteworthy that Frommel, in his essay entitled *Ueber puerperale Atrophie des Uterus*, referred to a description of the syndrome by Chiari in 1855.² Two contemporary clinicians, Simpson³ and Schröder,⁴ were cited by Frommel as having been cognizant of the syndrome. Since Chiari might be properly accredited with the initial description of the symptom complex, his original observations will be given in their entirety.

Chiari, with the collaboration of C. Braun and J. Spaeth, published a series of essays on gynecologic and obstetric subjects embracing observations on patients in the clinics of Vienna during the years 1848 to 1855, inclusive. In a subsection of one of Chiari's reports there appears under the title: "Anomaly of size," a description of various types of uteri. In a sketchy, disconnected form of annotation, made more difficult to interpret because of a mixture of archaic, classic, and colloquial idioms, he discussed two cases of puerperal uteroovarian atrophy accompanied by persistent lactation. After commenting briefly on the flaccid, atrophic, and deviated uteri found in chlorotic women, Chiari asserts:

To the acquired uterine atrophies belong two cases described below which were associated with persistent secretion of milk following their puerperiums, causing also complete amenorrhea despite the youthful age of the patients.

Case 1, patient 36 years of age, married, gave birth to a baby girl 8 years ago without complications. The baby was breast fed for several months, during which period the menses did not appear, but a moderate degree of lactation continued. The patient noted also that she became obese. Upon examination a watery milk-like secretion was expressed from her breasts, a small portio vaginalis and a very thin, relaxed uterus were disclosed. The uterine cavity measured about 5.08 cm. in length.

Case 2, patient 28 years of age, delivered normally and at full term 14 months before (first pregnancy). After nursing her baby for three weeks she menstruated at regular intervals for two periods, followed by amenorrhea. Since then she complained of general abdominal pain, moderate during the day but very severe during

the night. Patient also noticed pressure on the breasts caused excretion of a thick, yellow-white milk. On vaginal examination there were revealed an atrophic, prolapsed, lacerated, patent cervix, and a very thin, relaxed uterus of ordinary length.

Chiari comments on these two case histories very briefly as follows:

Leucorrhœa (blennorrhœa) was not observed in either case before or during the observation. We look upon both as early senile atrophy of the uterus which depends upon the nutritional state of the patient and is more or less influenced by general health.

After reviewing Chiari's brief and informative communication, the failure to recognize the clinical import of the symptom-complex until Frommel's fortuitous essay in 1882 is astonishing at this advanced period.

The opening section of Frommel's essay was devoted to a review of the literature and citations of opinions about the classification, incidence, pathogenesis, and diagnosis of various types of uterine atrophy. Because of his pertinent statistical data and the accurate description of the puerperal syndrome, a slightly abridged translation of his report is subjoined:

Among 3,000 gynecologic patients, 28, or about 1 per cent, showed various types of uterine atrophy. It is of especial interest that atrophy is not limited to women of middle age, who after a great number of pregnancies develop atrophy of the uterus. Of the 28 cases, one patient 19 years of age showed this condition, and the eldest patient in the group was 40 years of age. The average was about 29.6 years. As a rule the women are young and poorly nourished and at first glance do not appear to be in their twentieth year. They come to the physician not because of amenorrhœa, despite the fact that breast feeding has been discontinued for several months, but because of a great number of complaints. Abdominal pain, sensations of active movements in the abdomen, backache over the entire back and extending down both legs, and numerous hysterical manifestations are among the symptoms. They are distressed and show mental depression.

The inspection of the external genitalia is, as a rule, negative. No inflammatory changes are present in the uterine adnexa, the ovaries are free and movable, but uterine atrophy is always found. In a few cases the uterus is much smaller, extraordinarily thin, length decreased (5 to 5.5 cm., in one case only 4.5 cm.) and generally firm and palpable. The atrophy effects the cervix, also, which is visible as a small peg in the vagina, or similar to senile atrophy, may be entirely absent. In other cases the uterus is not shortened, but there is a change in the thickness of the walls, so that palpation is often difficult. The uterine body is generally mobile and can be moved from the anteverted to the retroverted position, but this type is usually in the retroposition. The vaginal cervix is often thick and firm but sometimes atrophic and flaccid. In introducing instruments care must be exercised to prevent piercing the uterine walls.

In the majority of cases the ovaries are small and atrophic. Only 3 cases out of 28 showed ovaries of normal size. Menstruation did not reappear in all cases after weaning. In one case the menses resumed for a short time, but amenorrhœa ensued. The condition may be caused or at least aggravated by lactation.

Frommel at this point advises breast feeding and describes his findings derived from examination of nursing mothers, concluding that a firm, small uterus is characteristic during lactation. He continues the thesis with these interesting observations on uterine atrophy:

These findings (on normal nursing mothers) support the assumption that in some women, as a result of lactation, the uterus attains such a pronounced degree of involution that a subsequent *restitutio in integrum* cannot occur. This may explain why atrophy is found among women after one or several pregnancies. Atrophy was found in 9 after 6 pregnancies, in 2 after 2, in 6 after 3, in 4 after 4, in 4 after 5, in 1 after 6, in 1 after 7, in 1 after 8 and 1 after 9 pregnancies. In all cases normal menstrual periods were observed.

In one case a young and robust woman developed a marked genital atrophy after her first pregnancy although lactation did not appear. Another woman, 23 years of age, gave birth to a premature baby (6 months) but resumed menstruation three months after delivery, having two scanty periods then ceased for a period of two years. Neither the history nor the examinations disclosed any cause to explain an atrophy of the uterus. A third interesting case was a woman, 28 years of age, who had given birth to five children, the last pregnancy having occurred one and a half years ago. After nursing the baby three months, breast feeding was discontinued, and the menses appeared for three months then ceased completely. Lactation persisted, however, from both breasts so profusely that her underwear and dress were always saturated. This condition continued for one year, and the patient found it necessary to wear two large towels to protect her clothes. Pressure on the breasts expelled an appreciable spray of milk. The uterus was slightly retroposed, 5.5 cm. in length, and thin-walled. Both ovaries were small and atrophic. The condition was still unchanged when this paper went to press.

Frommel concluded that women who experience numerous pregnancies in rapid sequence have imposed on the genital organs a great biologic demand, which may contribute to uterine atrophy. He expressed the belief that the prognosis in genital atrophy due to prolonged lactation was unfavorable, since only one of his 28 cases showed complete recovery. Prophylaxis was recommended—detection of abnormal involution early in the puerperium followed by immediate weaning of the infant. His outline of therapy embraced hot sitz baths, improved nutrition, insertion of pessaries to irritate the uterus, and iron for the anemia.

COMMENT

Malnutrition in the inhabitants of the large centers of population in Central Europe during the periods Chiari and Frommel made their observations may have contributed to the incidence of this or any other disease. In any event, the prevalence of the puerperal syndrome was not alarming since less than 1 per cent of three thousand women displayed the same symptomatology.

The rarity of the entity is not so intriguing as its endocrine implications. Mammary function is identified with anterior pituitary control, as is the gonad, while all are physiogenically involved in gestation. A

clear delineation of the mechanism responsible for the precipitate genital changes and persistent postpartum lactation could not be undertaken under any circumstances, however, without data on the antepartum integrity of the ineretory system. Pregnancy alone is presumptive but not conclusive proof of normal balance in the reproductive zone.

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PREGNANCY COMPLICATED BY CARCINOMA OF THE CERVIX

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THIS report owes its inception to the study of six patients with pregnancy complicated by carcinoma of the uterine cervix met with in this hospital. I propose to present their histories, with the method and results of treatment. Not knowing definitely the viewpoint and practices at other clinics, I have undertaken a review of the literature and, with but few exceptions, found little detail. It consists mostly of observations in one or more individual cases with little or no discussion as to the best method of treatment for this condition as a whole. The vast majority were treated by complete hysterectomy in the earlier months of pregnancy and, after the seventh month, by cesarean section and hysterectomy. Only an occasional instance is reported where radiation alone was used, but considerable advice against such treatment on account of the harmful effect on the offspring. I can find but scanty mortality statistics following the complete operations, but the average of my findings is high.

Fortunately the condition is rare. Stöckel reports that out of 18,000 pregnancies there were 8 cancers of the cervix, or 0.04 per cent. Kerstner's percentage is 0.05 per cent. Hirst in a group of 12,484 pregnancies found only 1 cancer of the cervix, or 0.008 per cent. Gross finds 1 cancer of the cervix in 1,538 pregnancies, or 0.065 per cent. Mendel in 29,962 pregnancies collected from the literature found 24 cancers of the cervix, or 0.08 per cent. In 1,500 pregnancies at the Johns Hopkins Hospital, there were 5 cancers of the cervix, or 0.3 per cent. Among 18,243 pregnancies at the University of Chicago there were two cervical cancers, or 0.01 per cent. In our own material, consisting of 2,703 cancers of the cervix, there were 6 pregnancies, or 0.2 per cent.

The incidence of occurrence is met with in the same relative frequency in primiparas and multiparas as is cervical cancer without pregnancy. The youngest

patient (sixteen years old) is reported by Tuft; an extensive condition ending in death to both mother and fetus without interference at the fourth month. Mylvaganam and Blonstein each reported an instance of twins at term, and Watson, triplets at the fifth month.

There is a divergence of opinion as to whether pregnancy stimulates or inhibits cancer. Such observers as Zweifeld and Simpson feel that it increases activity, while Weibel, Wolfe, Meyer, and Stöckel are of the opinion that it retards the growth. On the contrary, Bumm, Hoffmeier, Kobak, and Cullen do not believe there is any effect one way or the other.

The diagnosis should not be difficult. The error frequently made is to consider all abnormal bleeding during the early stages of pregnancy as a threatened abortion and, in the later months, as placenta previa or some type of accidental hemorrhage. The general tendency against making a pelvic examination during pregnancy should be changed, thus preventing an occasional cervical cancer to progress undiagnosed. Much can be learned from a rectoabdominal examination, coupled with a direct inspection. The hesitancy in doing a biopsy undoubtedly is due to its improper performance, the tendency being to remove too great an amount of tissue, necessitating the cautery or suture to check bleeding, with a later possibility of infection. The more simple procedure, fraught with no danger of complication, is adequately accomplished by removing without anesthesia a small bit of tissue with a nasal rongeur forceps from a characteristic area of the erosion with the patient on the office examining table. The patient is able to return at once to her home, and an accurate diagnosis is established.

Considerable has been written as to the effect on the offspring, both where radiation has been given prior to conception and after pregnancy has occurred. In patients treated by radiation followed by a temporary amenorrhea, with a later return of normal menstruation, pregnancy rarely occurs, but should conception take place, there is a marked tendency to miscarriage. Goldstein and Murphy in a study of 650 pregnancies associated with pelvic radiation prior to conception found 24 per cent ended in abortion and 13 per cent in the birth of defective children. From a study of reported cases, it is not clear whether this is a direct result of the radiation, or due to the condition for which the patient was originally treated. It has been definitely determined, however, both by experimentation on animals and from the observation on human beings, that radiation after pregnancy has occurred has a definite tendency to injure the offspring, and because of this, therapeutic radiation during pregnancy should not be carried out unless all other methods of treatment have been carefully considered.

Mendel collected 12 cases from the literature where radiation was used during some stage of pregnancy, with birth by cesarean operation of normal children at term, and 15 others wherein there was definite injury, 4 ending in abortion, 6 at term with

intercranial abnormalities, and 5 malformations. Goldstein in a study of 24 radiated pregnancies reports 16 unhealthy children, and he advises that a pregnant uterus should never be radiated.

It is my opinion that radiation is a much more efficient method of treating cancer of the cervix complicated by pregnancy than any radical operative procedure. The treatment should be instituted just as soon as the diagnosis is made. In the first four months of pregnancy it is hardly possible to radiate without injury to the fetus, and the entire endeavor of the treatment should be directed toward curing the cancer and saving the life of the mother. In the later months it is not only possible to cure the cancer but also to obtain a normal child, by the topical application of radium. It is safe to give in a single application from 3 to 3.5 gm. hours, the technic followed being almost identical with that used in cancer of the cervix not complicated with pregnancy. The patient is placed in the knee-chest posture which, with a Sims speculum, allows full distention of the vaginal cavity and perfect exposure of the entire growth. The radium, held in a cloth form, containing from six to eight separate tubes, is folded over the entire surface. Lead screens are interposed, protecting the bladder and rectum, while the vaginal cavity is packed lightly with sufficient gauze thoroughly to displace all normal mucous surfaces away from the radium. A large amount of radium is used in each instance, the total being from 2 to 3 gm. and the actual time of application is not over one to one and one-half hours, which eliminates any possible dilatation of the cervix that might occur from the packing. We do not place tubes in tandem within the cervical canal to the level of the internal os as is the routine in patients without pregnancy. Careful follow-up examinations are made until after the birth of the child and further treatment given, either through the cervix with radium or externally about the pelvis with x-ray, should it be indicated.

In the early months of pregnancy, should the irradiation not cause abortion after the growth is thoroughly under control, it should be produced by mechanical means. In the later months it is advisable to allow the pregnancy to proceed to term, ending it by cesarean section. The operation should not be any type of a Porro, nor should an attempt be made to remove the uterus. The poor immediate results and high operative mortality from the complete operation would indicate radiation treatment, as outlined, to be the better plan.

CASE REPORTS

CASE 1.—*Operable carcinoma of the cervix with pregnancy at the fifth month.* Mrs. M. B., white, aged thirty-two years (No. 22599). Previously she had given birth without difficulty to three children. She was first seen May 13, 1930. There had been irregular vaginal bleeding for the past three months and, prior to pregnancy, a chronic leucorrheal discharge. Past history was negative for serious illnesses or operations. On examination, occupying the anterior half of the cervix there

was a large everted, fungating mass, and induration at the base of the right broad ligament, without fixation; left side clear. Hemoglobin was 56 per cent. Child was viable. Tissue diagnosis, squamous cell carcinoma, Grade III. A topical application of radium was given against the growth of 3,109 mc. hours. All bleeding ceased after one week. Next seen July, 1930; pregnancy advancing normally and the cervical growth healed. On Sept. 12, 1930, a normal child, weighing 8 pounds, was delivered by cesarean section. An examination of the lateral pelvic structures intraabdominally revealed no evidence of extension of the growth. In March, 1931, the patient's gallbladder was removed for an upper abdominal condition. Six months after delivery normal menstruation returned and continued until July, 1931, when she was given treatment with x-ray for a total of one E. S. D. over front and back of pelvis to establish an artificial menopause. This was satisfactorily brought about and at present there is no palpable evidence of the carcinoma. The child, four and one-half years old, is perfectly normal.

CASE 2.—*Operable carcinoma of the cervix with pregnancy at the sixth month.* Mrs. A. W., white, aged twenty-nine (No. 24792). First seen Nov. 28, 1931. Past history negative for serious illnesses or operations. She had two living children and two miscarriages. Chronic leucorrhea had been present for years. First noted irregular bleeding in January, 1931, four months before pregnancy occurred and continued in scanty amount without cessation until August, 1931, when the bleeding increased and treatment was instituted for threatened abortion. On examination there was a friable bleeding mass on the posterior cervix; no lateral extension. Tissue examination, squamous cell carcinoma, Grade III. A topical application of radium was applied against the cervix for a dosage of 3.6 gm. hours. Labor began Feb. 11, 1932, when a cesarean operation was done with the delivery of a normal 8-pound baby. At the time of operation palpation within the pelvis failed to reveal any evidence of intrapelvic malignancy, and the cervix was healed. Jan. 19, 1935; mother and child both healthy; no evidence of any cancer. Normal menstruation occurred six months ago and has been regular ever since. X-radiation over the pelvis for an artificial menopause was advised which so far has been refused.

CASE 3.—*Operable carcinoma of the cervix with pregnancy at seven and one-half months.* Mrs. O. H., colored, aged twenty-eight (No. 17355). First seen Dec. 1, 1926. Past history was negative as to serious illnesses or operations. There had been four normal pregnancies. Scanty vaginal bleeding began in September, 1926, which was continuous until I saw her, and during this period, she was treated for threatened abortion. Health continued good and she gained in weight as the pregnancy advanced. On the right side of the cervix was a solid, nonulcerating, rounded tumor, bleeding on touch. The cervix was movable with the fundus, and the fornices were clear. The tumor, with the cervix, could be delivered entirely outside the vagina, and was removed with the cautery. Tissue revealed squamous cell carcinoma, Grade III. On Dec. 15, 1926, four glass radon capsules, each containing 2.5 mc., were implanted permanently into the cervical stump and on Dec. 18, 1926, 1,765 mc. of radon topically applied. The pregnancy continued its normal course, with cessation of bleeding, until Jan. 16, 1927, when her first labor pains began and a healthy female child, weighing 6 pounds, 4 ounces, was delivered by cesarean section. On April 1, 1927, a superficial but definite metastatic nodule 1 cm. in diameter was removed from the right vaginal orifice with the cautery. The patient remained well without return of menstruation until January, 1931, when there was a definite mass in the right femoral region, the pelvic structures remaining perfectly clear. In May, 1931, there was a profuse hemorrhage from this sloughing mass, occurring at her isolated home in the country, and she died before a physician could reach her. The child is well and over eight years of age.

CASE 4.—*Extensive, inoperable carcinoma of the cervix with pregnancy.* H. M., colored, aged thirty-eight (No. 24279). First seen on June 5, 1931. She had three normal children; one miscarriage. There had been no complication with the present pregnancy until the fourth month, when a scanty, irregular, bloody vaginal discharge appeared which continued. For years there had been a chronic leucorrhea. Past history was negative for serious illnesses or operations. On examination, cervix occupied by a large, craterous ulceration, with involvement in the right broad ligament region all the way to the pelvic wall, and to a lesser extent on the left. Tissue diagnosis: squamous cell carcinoma, Grade III. A cesarean section was done the following day, with delivery of a normal child. On July 12, 1931, a topical application of radium was given against the cervix of 3,000 mc. hours, and a series of deep x-ray treatments through multiple portals about the pelvis, completed July 30, 1931. Sept. 27, 1931, the condition was no better. Sept. 30, 1931, one gold radon capsule, 13.6 mc., was implanted permanently into the cervical growth, and on Nov. 15, 1931, an additional 1,000 mc. hours applied against the cervix. There was little, if any, general improvement, but definite relief from pain and hemorrhage. Death occurred from the disease on April 23, 1932.

CASE 5.—*Extensive carcinoma of the cervix with pregnancy at term.* Neglected for one and one-half years. Mrs. E. F., white, aged thirty-nine (No. 24280). Past history was negative as to serious illnesses or operations. She had six children; two miscarriages. On Dec. 10, 1929 she was delivered elsewhere of a normal child by cesarean section followed by supravaginal hysterectomy. On account of irregular bleeding, while in the hospital, the cervix was examined and tissue removed, which revealed squamous cell carcinoma, Grade III. No attempt was made to do anything for this condition and she was discharged. The bleeding continued in small amounts without symptoms until September, 1930 when it became profuse and she consulted another physician and was told she had change of life, and nothing was done until July, 1931 when, due to the continuation of bleeding, she was sent to this hospital. On examination cervix was replaced by a huge, fungating mass, nearly filling the vaginal cavity, with complete fixation from side to side. Palliative x-ray treatment given July 25 and 26, and on August 3, 3,000 mc. hours radium radiation given against the cervix. This checked the bleeding and made the patient more comfortable, but she died of the disease on Sept. 4, 1931.

CASE 6.—*Extensive carcinoma of the cervix with pregnancy, spontaneously delivered at term.* Mrs. T. K., white, aged thirty-five (No. 23125). Past history negative for serious illnesses or operations. She had ten children. Suffered from chronic leucorrhea for years. In April, 1930 at the fifth month of pregnancy there appeared an irregular bloody vaginal discharge. On Aug. 24, 1930 she was delivered spontaneously, with considerable difficulty and hemorrhage. The baby lived three days, its death being due to a malformation of the esophagus. Nothing further was done, the opinion being that the condition was hopeless. Due to pain and bleeding I was asked to see her on Sept. 30, 1930. On examination patient was pale and ill and the vaginal cavity almost entirely filled with a large, fungating growth, with fixation to both broad ligaments and base of the bladder region. On Oct. 2, 1930 the large fungating mass was removed with a dull spoon curette, and it was felt that she would develop a vesicovaginal fistula. Tissue diagnosis: squamous cell carcinoma, Grade III. On Oct. 4, 1930 a topical application of radium was given against the growth for a dosage of 3,000 mc. hours. Astonishing improvement immediately followed and in July, 1931 everything was healed at the vaginal vault, but there was still fixation laterally. On July 18, 1931 an additional 1,000 mc. hours radium radiation was given against the vaginal vault for a recurrent ulcer, showing active

cancer. She remained symptomatically well until December, 1933 when extensive recurrence was noted locally and 1,400 mc. radium hours were given against the recurrence, checking the bleeding and affording comfort to the patient, but her general condition declined, and a vesicovaginal fistula developed in February, 1934, which persisted until her death of the disease in July, 1934.

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Mitsui studied 230 appendices removed during the course of gynecologic operations. He found a stricture of the appendix in 24 cases. There was evident decrease in the mobility of the cecum in 27 cases, and 25 of these had complicating appendicitis. There was excessive mobility of the cecum in 17 cases and only 8 of these had associated appendicitis. The author found bacteria in 91 per cent of all the appendices; he also studied the tubes and ovaries of 53 of these cases and found bacteria in 19 of them. He failed to find any direct connection between the lymphatics of the appendix and the female genitalia as claimed by Clado and Durand.

In the series of 230 cases, the appendix was found diseased in 143 cases. Hence there is a definite relationship between appendicitis and gynecologic disease. Cystic degeneration of the ovaries occurred in 30 per cent of the cases. Furthermore, 53 per cent of all these patients were sterile, hence there is a definite connection between sterility and appendicitis. In addition, there were 21 cases of ectopic pregnancy, 8 of which complicated appendicitis.

The author believes that when women of marriageable age have an attack of appendicitis the appendix should be removed even if the attack is slight.

J. P. GREENHILL.

TUBERCULOUS ENDOMETRITIS

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TUBERCULOSIS of the female genital tract is in itself not as common as generally supposed. Tuberculosis of the endometrium, diagnosed as an isolated lesion from the uterine curettings without demonstrable pathology in the tubes or in the cervix, can safely be assumed to be an uncommon lesion.

In the Department of Pathology of our hospital, receiving approximately 4,000 fresh tissues from the surgical service each year, among which there is a yearly average of about 500 gynecologic specimens, tuberculosis of the genital tract has been found only thirty times during the last seven years, or in about 0.85 per cent. Tuberculosis in the endometrium has been observed but once.

Dickinson¹ is of the opinion that most lesions are secondary and descending and that the endometrium is involved in about 40 per cent of genital tuberculosis. Gupta² believes that when the corporeal endometrium is involved the tubes are nearly always infected. He states that tuberculous endometritis is rarely diagnosed clinically because of the difficulty of demonstrating the bacillus in the discharges, and he prefers curettement for differential diagnosis. He reported six cases of cervical and corporeal tuberculosis, two of which seemed to be primary in the cervix. Reinhart³ found tuberculosis comparatively rare in genital pathology. He cites Fromme and Heynemann who found genital tuberculosis in 142 of 17,470 autopsies, or about 0.81 per cent and Schlipfert who found 3.4 per cent of genital tuberculosis in tuberculous women and children. Reinhart reports two cases.

The infrequency of endometrial involvement has been explained by some writers as due to the physiology of the uterus with its periodic desquamation, making bacterial rests difficult of maintenance. This is questionable as the mucosa does not entirely desquamate during menstruation. Trauma, previous infection, and pathologic changes interfering with the menstrual function are credited as being etiologic factors. Clinical symptoms, unless associated with frank tuberculosis elsewhere, when the diagnosis can be made by inference only, are not particularly illuminating: nor are the findings on examination. Demonstration of the microorganisms or the characteristic tubercles in uterine curettings or in cervical biopsies seems to offer the only certain means of diagnosis previous to generalized pelvic tuberculosis calling for laparotomy.

CASE REPORT

Mrs. P. C. G., aged twenty years, white, one child, one miscarriage. There were three admissions to the hospital. Jan. 15, 1933: She was admitted by her physician for incomplete abortion. Her pregnancy was of two months' duration. There was no intrauterine manipulation, and after spontaneous evacuation, the patient was sent home cured. On Aug. 23, 1933, she was again admitted complaining of menorrhagia and dysmenorrhea. The periods were of twelve days' duration and excessive in amount with some premenstrual discharge. Her past history revealed pneumonia, diphtheria, tonsillectomy, and appendectomy. Her general health had

been good and she had been leading a very active social and athletic life. Weight about seventy-two pounds. Height five feet two inches. A careful pelvic examination showed a small, firm, freely movable uterus, normal in contour, and in good position. The adnexa were not palpable nor tender. There was a slight cervical erosion with bilateral laceration of the cervix and some hypertrophy. The introitus was parous, and the perineum in good condition. No lesions were noted on the vulva or the vaginal mucous membrane. The urine was negative except for an occasional pus cell. The blood showed hemoglobin 69 per cent, R.B.C. 3,350,000, W.B.C. 6,450; polymorphonuclears 66 per cent, lymphocytes 30 per cent, monocytes 3 per cent, transitionals 1 per cent. Wassermann and Kahn negative. Metabolism reading was -9.

A diagnostic curettement was done and microscopic examination of the curettings showed numerous typical tubercles as well as the tubercle bacillus.

A roentgen examination of the chest showed the chest symmetrical, heart somewhat rounded, hilus shadows increased, increase in the linear markings on both sides, most marked on the right side with a suspicious area in the second interspace posteriorly on the right. However, this did not appear active.

The pulse, temperature, and respiration range remained normal. She was discharged on the seventh day with the diagnosis of miliary tuberculosis of the endometrium. The condition was explained and extirpation was advised, but was refused by the patient and her husband on the grounds of comparative health and lack of convincing discomfort.

Oct. 10, 1933, admitted for hysterectomy. Following her discharge in August there had been almost daily bloody discharge. General health was good until one week ago, when there was abdominal pain of dull character radiating down the legs, made worse on standing and on walking. She also had a "cold," with coryza and slight cervical adenopathy. Physical examination was much the same as on previous examination except for the pelvic findings, and here a great change was observed. The uterus was fixed in the pelvis. There were bilateral tender masses fairly soft in consistency. The cervix was little changed, the erosion being about the same. The temperature, pulse and respiration range were normal. The urine showed traces of albumin and few pus cells. The hemoglobin was 87 per cent, R.B.C. 4,510,000, W.B.C. 9,550. A diagnosis of pelvic tuberculosis was made, and a complete hysterectomy with bilateral salpingo-oophorectomy done (M. W. Diethelm).

The peritoneum was found studded with tubercles. There was a small amount of pale fluid in the pelvis, and the uterus and adnexa were bound down by an exudate and recently formed adhesions. The tubes were large, thickened, and tortuous. Both ovaries were cystic. The uterus, cervix, tubes, and ovaries were removed.

TABLE I. SHOWING TUBERCULOSIS FOUND IN GYNECOLOGIC SPECIMENS EXAMINED IN ST. VINCENTS HOSPITAL PATHOLOGICAL LABORATORY DURING THE LAST SEVEN-YEAR PERIOD*

	1927	1928	1929	1930	1931	1932	1933	TOTAL
Tuberculous specimens	2	10	3	5	3	3	4	30
Tubes only	2	7	2	4	2	3	3	23
Tuboovarian		3	1		1			5
Ovarian only								0
Tubes and broad ligament				1				1
Endometrium								0
Cervix, tubes and endometrium							1	1
Total number gynecologic specimens	501	558	603	507	578	477	423	3647

*Percentage of tuberculosis found 0.85.

en masse, and the vagina and abdomen were closed without drainage. Convalescence was uneventful except for an allergic reaction to luminal. She was discharged on the twenty-first day. She has been examined twice since the operation and the pelvis is free from induration, masses, or tenderness. She is in good health and has

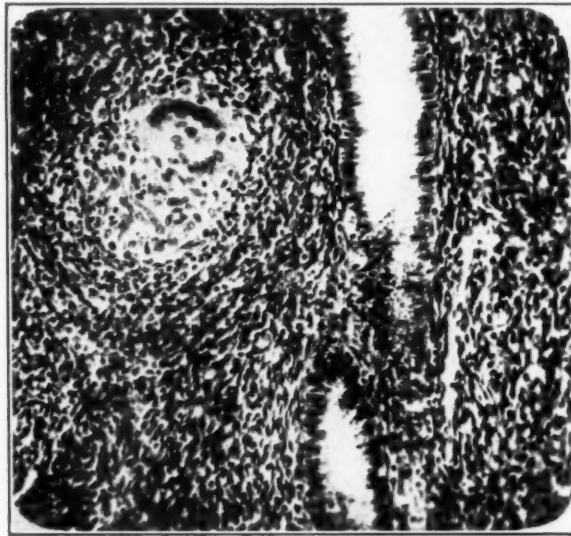


Fig. 1.—Microphotograph showing typical tubercle as seen in curettings for diagnosis. $\times 100$.

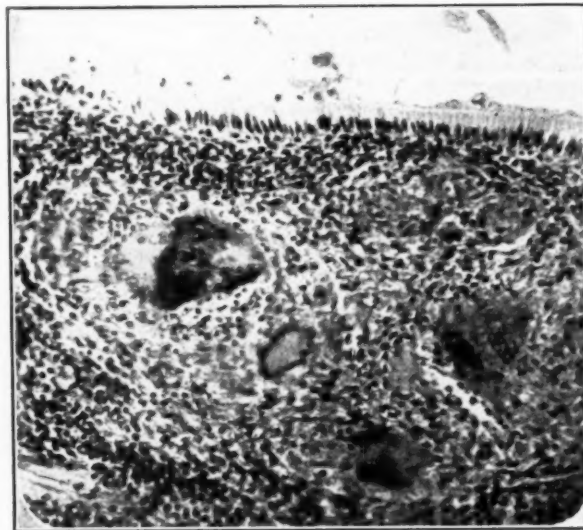


Fig. 2.—Microphotograph, cervix after hysterectomy showing coalescing tubules in stroma between gland crypts. $\times 100$.

gained some 34 pounds. Her physician reported in October, 1934, that she is apparently cured.

The specimen was examined grossly and microscopically and microphotographs made (T. Ramsey), the description of which follows:

Gross.—The specimen included the uterus, cervix, both tubes, and both ovaries. The cervix was small, rather irregular in shape and showed erosion at external os. The mucosa of the canal was thickened and congested. The uterus was small, measuring 8 cm. in length by 4 cm. across the fundus; the wall showed a moderate fibrosis; the

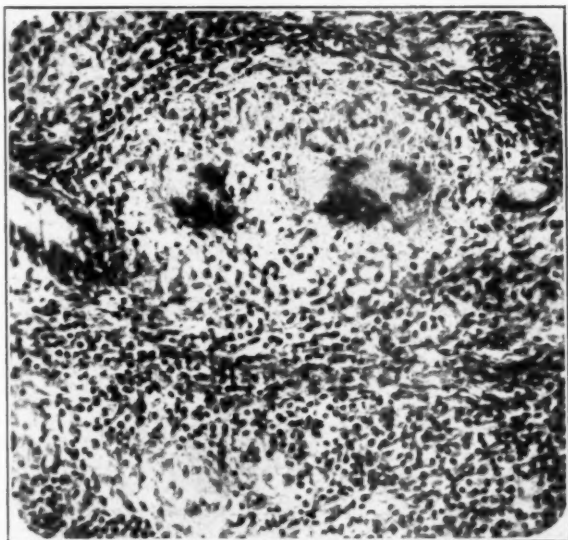


Fig. 3.—Microphotograph showing tubercles in residual endometrium after curettage. Sections taken following hysterectomy. $\times 100$.

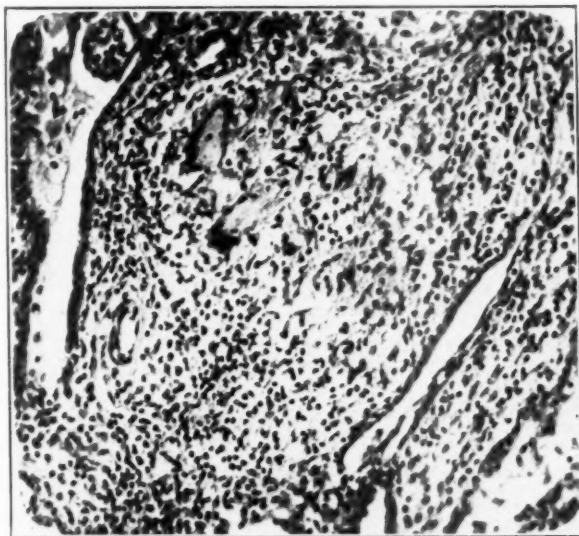


Fig. 4.—Microphotograph showing tubercle in thickened folds in fallopian tube. $\times 100$.

endometrium was edematous and appeared to be thickened especially in the fundus. The tubes were constricted at the uterine ends and were markedly congested, the largest measuring about 16 cm. in length by $2\frac{1}{2}$ cm. in diameter at the fimbriated end which was occluded. The other tube was very tortuous and measured 11 cm. in

length. Upon cutting into the tubes, they were seen to be distended with pus which was of a thick yellow consistency. The tubal ligaments were thickened. The ovaries were enlarged and partially destroyed by multiple cyst formations. The peritoneal surfaces of both tubes and ovaries appeared somewhat granular. There was a granular appearance on the peritoneal surface of the fundus uteri. Sections were taken from the cervix, fundus of the uterus, and from the ovaries and tuboovarian ligaments.

Microscopic.—The cervix showed chronic ulceration at external os with considerable scar tissue formation. The exposed surfaces showed round cell infiltration and a few tubercles in the granulation tissue. The uterus showed fibrosclerosis, and the mucosa was thickened and contained numerous actively developing tubercles with epithelioid and giant cells. The glands were irregular and somewhat distended, forming small cysts. The tubes showed dense infiltration with inflammatory cells, and the folds were thickened and filled with developing tubercles, practically obliterating the tubal lumen. The tuboovarian ligament was thickened and showed productive inflammation with numerous tubercles. The ovary was cystic and sclerotic. No tubercles were seen in the ovarian substance or developing upon its surface. The peritoneum over the tubes, ligaments, and fundus of the uterus showed developing tubercles in and upon its surface.

Diagnosis.—Active tuberculosis involving the cervix, endocervical mucosa, mucosa of the uterus, folds and walls of the tubes, tuboovarian ligaments, and peritoneum over the surface of the pelvic organs. The ovaries were uninvolved but showed fibrosis and cystic degeneration. Tubercle bacilli were found in the giant cells.

Comment.—This case is presented because of its unusual features, and because of the rarity of tuberculous endometritis. Our impression is that it is an ascending infection, and primary in the cervico-uterine canal extending after curettement to the pelvis. We are led to believe that by careful and perhaps by repeated curettements preferable during the midinterval period, a differential diagnosis can be made. An early diagnosis with complete hysterectomy would anticipate the pelvic extension and allow the conservation of the ovaries in the ascending type. It would seem that since the tubes are so quickly involved, they should always be removed with the uterus even if not visibly affected. In our case the interval between the initial diagnosis, when operation was advised, and the time when the subjective symptoms forced the acceptance of surgical relief, was but six weeks. The pelvic touch picture changed from apparently negative to one simulating the so-called "frozen pelvis."

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From a study of the literature and from his own investigations, Schumacher comes to the conclusion that Ogino and Knaus are wrong when they maintain that women cannot possibly conceive during the few days of the premenstrual period. Schumacher firmly believes that the premenstruum is not an absolutely safe period but only a period when conception takes place with more difficulty than at other times in the menstrual cycle. He reports three carefully controlled cases which support his contention and oppose the belief of Ogino and Knaus.

J. P. GREENHILL.

MASSIVE COLLAPSE OF LUNG FOLLOWING CESAREAN SECTION

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POSTOPERATIVE massive collapse of the lung or atelectasis was first described as a clinical entity by W. Pasteur in 1910. In 1925 Scott reviewed all cases then reported, which were 64 in number. Of these 64 cases, only 38 were given in sufficient detail to permit analysis. Since this time many cases have been reported, chiefly by general surgeons, internists, radiologists, and bronchoscopists. Several of the reported cases have followed gynecologic operations. I noted one case of partial collapse following a cesarean section by Piper of Philadelphia, reported by Chevalier Jackson and Lee. This patient died on the third day, and autopsy showed postoperative collapse of the left lower lobe of the lung, partial atelectasis of base of right lobe with terminal localized peritonitis and paralytic ileus.

Collapse or atelectasis has developed in patients on whom operations had been performed under ether, nitrous oxide-oxygen, spinal, and even under local novocaine anesthesia. The purpose of the following report is to focus attention to its occurrence, diagnosis, and course, in the hope that we as obstetricians and gynecologists will permit fewer cases to go unrecognized.

CASE REPORT

M. C., a twenty-three-year-old primipara, first consulted me on Nov. 16, 1933. Menses had started at fourteen, had been very irregular and accompanied by considerable dysmenorrhea. Her last period began July 23, making her due April 30. Her father had died of pneumonia, and her mother, one sister, and one brother were living and well. She had had measles, whooping cough, a tonsillectomy, and an appendectomy. About a year ago, she had had insertion of a stem pessary for dysmenorrhea by a general surgeon. General examination was negative. External measurements were 25:27:32:19 and bi-ischial 9. Internal examination revealed a four months' pregnancy with no adnexal pathology. The promontory was rather easily reached, her C.D. measuring 12 cm. and C.V. estimated at 10.5 cm. Her entire prenatal course was uneventful with all findings within normal limits, until on April 12 she reported with a severe cold of a week's duration. I immediately sent her to her rhinologist for treatment, a measure strongly advocated by Lubin as prophylaxis against massive collapse. On April 20, 1934, she seemed well over her infection.

On April 25 the patient entered the Methodist Hospital with contractions every two to three minutes. These stopped at 4:00 A.M. on April 26, and active labor started at 11:00 P.M. on that date. After fifteen hours of trial labor, a cesarean section was advised because of disproportion. There was marked overriding of the head which was fixed, but not engaged, and could not be "impressed" to the spines, the baby being large and the pelvis slightly flat. The conditions present were: (1) patient in labor for fifteen hours, (2) B.O.W. intact, (3) fetal heart 144, (4) position O.D.T., (5) station—1, (6) dilatation 7 cm.

The patient refused local anesthesia. Her preanesthetic medication was sodium amytal gr. 6 and atropine sulphate gr. 1/150. A low cervical cesarean with transverse incision in the lower uterine segment was done, under nitrous oxide-oxygen anesthesia, given by a trained anesthetist of many years' experience. Morphine sulphate gr. 1/6 was given after the birth of the baby. The latter was a 9-pound boy. The patient was in good condition throughout the operation though she had a moderate amount of mucus. On waking she had some desire to cough. Her position was changed frequently, and the next day she continued to cough up thick mucus. On April 29, 1934, the patient complained of a feeling of compression in the upper chest and was coughing and expectorating thick pus. Her highest temperature had been 101.6° F., pulse 120, and respirations 24. On auscultation of the chest there were few breath sounds over the right chest, while those of the left were exaggerated. She was seen at 10:30 A.M. that day by her internist, Dr. Edgar

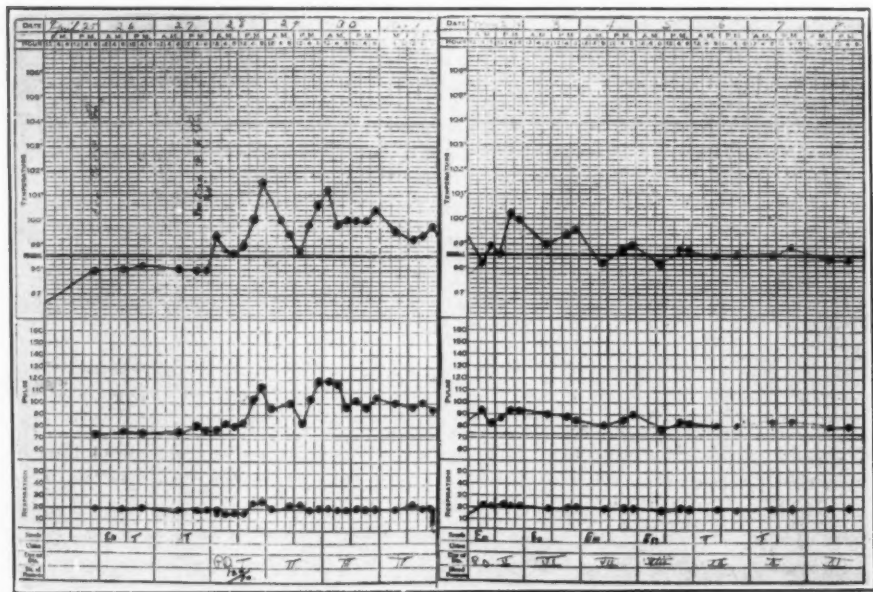


Fig. 1.—P. T. R. curves.

Kiser, who found dullness and impaired breath sounds over the right lung, posteriorly, and upper right lung, anteriorly. There were increased breath sounds over the left lung. At 8:30 P.M. there was complete absence of breath sounds over the entire right lung with the apex impulse of the heart in the midsternal line. Slight cyanosis was noted. With these findings, Dr. Kiser made a clinical diagnosis of atelectasis or massive collapse of the right lung. Symptomatic and postural treatment, as outlined by Sante, was decided upon.

Thick greenish pus was expectorated by the patient until May 3, and was usually the result of paroxysms of coughing. Blood counts were as shown in Table I.

Progress of the patient can best be shown by the P.T.R. curves (Fig. 1) and the roentgenograms taken at her bedside. The first one taken on April 29, 1934, is shown in Fig. 2. This demonstrates a gross pathologic change on the right side, characterized by obscuration of the right leaf of the diaphragm, and a smooth, homogeneous density over the entire right chest. The interspaces between the upper ribs appear to be definitely narrowed as compared with those on the opposite

side. The left lung is entirely clear, with the exception of an old primary healed specific focus in midlung field. The roentgenologist concurred in the diagnosis of atelectasis.

The second roentgenogram was taken on May 1, 1934 (Fig. 3). The right leaf



Fig. 2.—Roentgenogram taken on April 29, 1934.

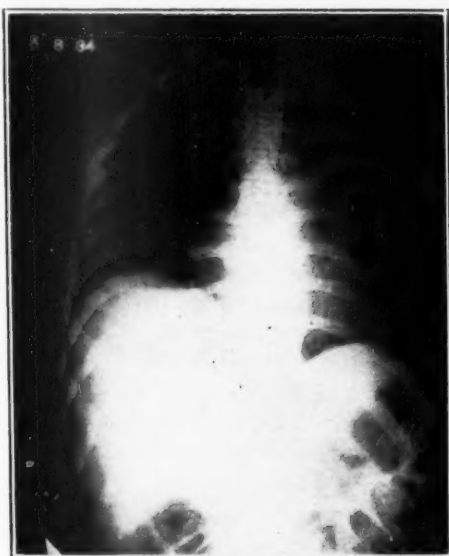
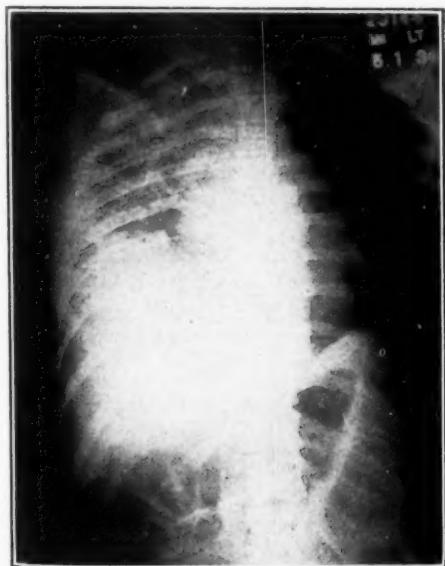


Fig. 3.—Roentgenogram taken on May 1, 1934. Fig. 4.—Roentgenogram taken on May 4, 1934.

of the diaphragm is markedly elevated, its position corresponding to the sixth interspace, posteriorly. The left occupies a position at the level of the ninth interspace. There is a gross pathologic change in the right chest characterized by marked increase in density involving the right lung. The left lung is clear. In comparison

with the study of Apr. 29, 1934, there is a very marked change in the appearance of the right chest. The right lung, previously entirely obscured, now appears partially aerated; the right leaf of the diaphragm, previously obscured, is now visualized.

TABLE I

	4/27/34	4/30/34	5/9/34
Hg.	60% or 11.2 gm.	58% or 11 gm.	67% or 11.3 gm.
Red count	3,380,000	2,990,000	3,260,000
White count	10,850	8,750	17,000
Polymorph	74	91	76
Eosinophiles	0	1	2
Basophiles	0	0	0
Small lymphocytes	25	8	10
Large lymphocytes	0	0	5
Mononuclears	1	0	1
Myelocytes	0	0	5
Polys			
Band	4	4	0
Bilobed	0	3	0
Adult	96	93	100

The third roentgenogram was taken on May 4, 1934 (Fig. 4). In comparison with the study of May 1, there has been marked clearing of the previously described atelectasis of the right lung. The right leaf of the diaphragm, previously at the level of the sixth interspace posteriorly, is now at the level of the eighth rib. The cardiac and supracardiac shadows are still slightly retracted to the affected side. The left lung remains clear.

The patient continued to improve, and mother and baby left the hospital on May 11, 1934, in good condition. At the present time the patient seems to have made a complete recovery.

COMMENT

This case has shown the most typical findings and course in atelectasis. Prophylaxis should include treatment of sinusitis and oral infection, partial Trendelenburg position while operating, removal of mucus by suction, frequent change of position postoperatively along with carbon dioxide inhalations, and the wider adoption of local anesthesia. When the condition occurs, prognosis is favorable unless a pneumonic process develops. The majority of patients do well with expectant, symptomatic, and postural treatment. CO₂ inhalations are advisable. Occasionally bronchoscopy may be indicated. Atelectasis probably occurs more often than we realize, both postoperatively and in the puerperium.

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AN INSTANCE OF LIKE MONSTERS IN SUCCESSIVE PREGNANCIES

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LIKE monstrosities occurring in successive births to the same mother, in whom were manifest some of the malformations found in the offspring, is a fact clinically as well as embryologically significant.

L. G., aged twenty-three years, primipara, was admitted to the hospital Mar. 1, 1932. After seventeen hours of active labor, she spontaneously delivered an eight-month, well-developed, female infant, weighing 4 pounds 7 ounces. It lived approximately twenty-four hours. The mother had a harelip, cleft palate, and no nasal septum. These had been reconstructed. She had a justminor pelvis.

Autopsy.—There was considerable molding of the head. No nasal septum, there being a single, external nares. The left eye was larger than the right. On opening the skull, about 15 ounces of clear fluid were obtained. The brain tissue consisted of a frontal lobe, collapsed, in the anterior part of the skull. The posterior and superior portions of the cerebrum were missing. The ventricles were not covered with brain tissue. The convolutions of the frontal lobe were diminished in number and the medulla showed marked congestion of the blood vessels. The other findings were normal.

Diagnosis.—Porencephaly; congenital absence of nasal septum; left eye larger and more prominent than right; prematurity.

The patient was readmitted Feb. 24, 1933, about one year after the delivery of the first monstrosity. Her last period, she claimed, was Apr. 12, 1932, due Jan. 19, 1933. This made the pregnancy five weeks postmature—in a woman with a justminor pelvis. X-ray examination showed a marked disproportion between fetal head and maternal pelvis. These factors were considered sufficient indication for section. The infant, another female, lived several hours.

Autopsy.—The body was that of a white, female infant, 51 cm. long, weighing 8 pounds, with the head distinctly enlarged, and prominent frontal eminences. The eyes were sunken and very soft, set close together, being 1.5 cm. between the inner and 5 cm. between the outer canthi. The nasal septum was absent, there being a single central nostril. The fontanelles were widely open, the sutures gaping, readily admitting one to one and one-half fingers.

On opening the skull through the sutures, about 700 c.c. of clear, colorless fluid escaped. The brain was compressed downward and anteriorly so that it occupied but a small portion of the cranial cavity. The cerebral hemispheres were represented by a thin sheet of homogeneous, yellowish white material, measuring 0.5 cm. in thickness. The corpus callosum could not be made out. The two ventricles appeared as one large, circular opening, 3 cm. in diameter, communicating directly with the fluid noted subdurally. The third ventricle could be probed. The cerebellum was intact and of normal development, likewise the pons, the medulla, and the spinal cord. The optic nerves showed a normal chiasmic arrangement and ended in the small eyes above noted. The other organs were normal.

Diagnosis.—Porencephaly; hydrocephaly; maldevelopment of cerebral hemispheres; absence of nasal septum; close approximation of eyes; enophthalmos.

Two cases of porencephaly, with maldevelopment of the cerebral hemispheres, structural defects in the eyes, and absent nasal septums, occurring in successive pregnancies to the same mother, who, likewise had a deficient nasal septum, besides a harelip and cleft palate, are worthy of note. Clinically, at least, such an occurrence of so closely related malformations seems to point to a germ plasm defect, transmitted through the ova.

901 WASHINGTON AVENUE

A CASE OF CHONDRODYSTROPHIC NANISM WITH DELIVERY BY CESAREAN SECTION

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CHONDRODYSTROPHIC nanism also called chondrodystrophia fetalis (Kaufmann), achondroplasia (Parrot), chondromalacic micromelia (Kirchberg) is a congenital disease of the skeleton productive of a peculiar type of dwarfism which, according to Bangson, is "due to a defect in the formation of cartilage on the ends of the long bones." After this arrest of development of the long bones of the extremities, the patients affected with this disease show distinctive characteristics, such as disproportionally large head (usually of the brachycephalic type), relatively long trunk, depressed nose, trident hands, and dwarfed and curved extremities.

This condition has been recognized since the earliest recorded times. The artistic description of the gods of Bes and Ptha shows that the primitive Egyptians encountered this particular type of nanism. Although the disease was well recognized and its mental and physical shortcomings known, the separation of chondrodystrophy into a distinct type of deformity really dates from Parrot's description of the malady in 1878. Some years later, in 1892, Kaufmann, in a very interesting and extensive monograph, disclosed the essence of the disease.

Historical, histologic, pathologic, radiologic, and clinical treatises have been so numerous and so thorough that additional repetitions are not necessary. The purpose of this report is to present a case of achondroplasia in an adult, associated with pregnancy and labor, and to call attention to the peculiarities of this malady in relation to the sexual activities of adult women affected with the disease.

Chondrodystrophia in the adult is rare, and its association or coincidence with pregnancy and labor is still more infrequent. The textbooks of DeLee, Williams, Hirst, Dorland, Döderlein, Girol, Vignes, and Auvard make very little or no mention of the condition, and an extensive perusal of the literature at my command further confirms the conclusion. I believe that this is the first case reported from the island of Puerto Rico. The condition is unusual in the adult because very few achondroplastic children are born alive. Most of them die in utero or during delivery, and those born alive seldom reach maturity. Because of this high mortality it was believed that the disease was essentially fatal, but now we know that, although the prognosis is very grave in the severe cases, the lower gradations of the malady are not necessarily incompatible with life.

Porak, Kaufmann, Breus and others have showed that certain types of dwarfs in adults present chondrodystrophic modifications similar to those exhibited in the congenital cases. These patients have a very striking appearance. Their mental

faculties are usually normal. Sexual desire and sexual activities as a whole are comparatively normal. Their genital organs develop normally though Wagner has called attention to the fact that they are excessively developed. He found the uterus large and wide in some of his patients. The secondary sexual characteristics are manifest as a rule very early, usually at the age of ten years. Menstruation usually appears at the proper time, and its periodicity is normal. No abnormalities of the menopause have been reported. These women seem to reproduce easily. Rebatu has reported one case in which the patient was pregnant nine times. Abortions are not more frequent than in normal women. Pregnancy evolves normally until term in most cases. While pregnancy may be and usually is normal, the same cannot be said of labor because all of these women have pelvis narrow in all dimensions. In the average case the measurements are about two-thirds of the normal. Labor usually starts at term. The effacement evolves normally, but the dilatation is very slow and tedious, the membranes rupturing long before the dilatation is complete. Because of the serious dystocia character of these pelvises, delivery is impossible through the natural passages, and unless operative assistance is given, the patient becomes infected and dies. Porak, who has made an extensive study of this matter, was the first to give a full description of this particular type of pelvis. He has shown that there are two distinct types which can be distinguished definitely from the purely rachitic type, formerly placed in the same classification. In one, the main characteristic is the marked flatness of the superior strait, with a general contraction resulting in a reniform pelvis. The promontory in this type is high and prominent, and the sacrum, greatly inclined, lies in a nearly horizontal plane. The second type is very rare. Its chief distinction consists in a general contraction in the form of a triangle with the superior strait somewhat larger.

CASE REPORT

On the afternoon of June 25, 1934, a patient entered our maternity service, who because of her striking appearance, attracted the immediate attention of all the attendants. She was a twenty-year-old, fat, and extremely short woman at full term. Labor had started vaguely with weak, irregular pains, which came every two or three hours, lasting for about thirty seconds. Pelvimetry revealed a flat pelvis with a conjugate of 6.4 cm. An x-ray picture showed a flat, deformed pelvis with the fetal head unengaged because of great cephalopelvic disproportion. Urinalysis showed slight traces of albumin; the hemoglobin was 70 per cent (Dare), red cells, 4,140,000; and the coagulation time (Bogg), 2.5 minutes. A vaginal smear was negative for gonococci, and the Wassermann test was also negative. An immediate intraperitoneal hysterotomy was performed, delivering a male child who weighed 5 pounds 3 ounces. The baby was essentially normal.

CLINICAL HISTORY

The patient's father died two years previously in an accident. Her mother died ten years previously, cause unknown. Both the father and mother were normal individuals. The patient was the only child, but her mother had several abortions. Her past history was essentially negative. It revealed no trouble in walking or exercising. There was no history of trauma or osteopathologic heredity. She was married a year previously. Her husband, thirty years old, was tall and appeared normal. Menstruation began when she was fourteen years old; periodicity was normal, twenty-eight-day cycle, the flow was scanty, lasting three to four days with comenstrual pain for the first two days. She had never missed a period until this pregnancy, the last period occurring Sept. 13, 1933. The pregnancy had been uneventful in spite of the fact that she received no prenatal care.

The patient was forty-six inches tall. The head was of the brachycephalic type. The face had a squatty appearance and the nose was depressed. The trunk was practically normal, but the extremities were extremely shortened. The upper extremities reached only to the hip joints. The hands and feet were unusually small. The skin was coarse and dry. The deposition of fat was greater than average, especially in the abdominal and gluteal regions. The hair was normal in amount, appearance, and distribution. The finger nails were small and friable. The eyes, ears, nose, and throat were normal. Physiologic enlargement of the thyroid was present. The heart and lungs were essentially normal. The pulse was soft and regular, 90 per minute;



Fig. 1.—Photograph showing patient and baby beside a normal-sized woman.

blood pressure, 90/54. X-ray plates disclosed considerable lordosis of the spine, curving of the forearms, deformed wrist and knee joints and a small, flat, deformed pelvis with large obturator foramen, prominent sacrum, small flattened acetabula, and very short necks of the femurs. The muscles were well developed. The teeth were small but in good condition. The gums were normal. The abdomen was large, with a full-term pregnant uterus. The ovoid was longitudinal; the head was on the inlet, floating; the back was to the left and anterior; and the small parts were in the fundus. The fetal heart tones were audible 1 inch below and to the left of the umbilicus. External pelvimetry 18, 20, 21.5, 17. The vulva was small, and the vagina narrow with moderate discharge. The cervix was small, high, soft, and closed. The perineum was rigid and the outlet considerably contracted. The adnexa

and culdesac were normal. Vertex, L.O.A. The breasts were large and pendulous with erect and well-formed nipples.

The patient was of a highly nervous temperament; there were no pathologic reflexes. She was mentally competent, but her intelligence was below average.

COMMENT

This case presents the main clinical features and the most important radiologic characteristics of achondroplasia. It is remarkable inasmuch as it shows no secretory deficiency of the thyroid gland, no history of osteopathology, and no history of syphilis—three important causes which have been heralded by the majority of the students of this important subject in their interesting debates on the obscure etiology of this disease. The essential peculiarities of this condition in relation to the sexual activities, including pregnancy and labor, were not unusual. The patient was first seen when labor pains started. Her pregnancy had been uneventful, but labor was impossible through the natural passages because of the marked deformity and contraction of the pelvis. This constitutes the first case of this type reported in the island of Puerto Rico, where osteopathology and marked disturbances in growth are quite rare, possibly on account of the beneficial effects of the sunny climate.

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A TUBE FOR THE COLLECTION OF URINE UNDER ASEPTIC CONDITIONS

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OFTEN it becomes desirable in gynecologic and especially in obstetric patients to collect a specimen of urine which will be free from contamination by vaginal discharges and lochia and which will avoid the necessity for catheterization with its attendant disadvantages. To this end the use of a simple device is recommended.

The collecting tube consists of an ordinary bent adapter, such as is used in chemical laboratories, the tube being 150 mm. long and bent at an obtuse angle. The wide mouth of the tube has an internal diameter of 18 mm. This type of tube is standard chemistry equipment, and may be purchased for a few cents at any chemical supply house. A few tubes may be kept sterilized and ready for use.

The tube is used to collect urine directly from the female urethra as follows: The patient is placed in a dorsal recumbent position in bed, the knees bent and

elevated as for vaginal examination. The labia majora are spread apart, and the region about the external urinary meatus cleansed with water and cotton pledgets avoiding the vagina and all parts except the area immediately surrounding the meatus. The mouth of the previously sterilized collecting tube is pressed gently around the meatus so that the external urinary orifice lies in the mouth of the tube. The patient is permitted to urinate, the urine passing directly into the tube and being collected in a receptacle placed below the small open end of the tube. The specimen is then removed for analysis.

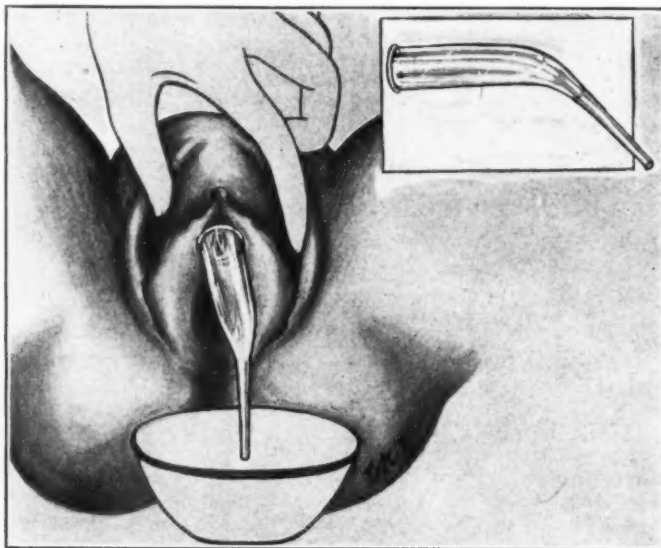


Fig. 1.—Collecting tube in place about external urinary meatus. Bent adapter used as collecting tube (insert).

Urine thus collected is received directly from the urethra into sterile containers, and all contamination from vestibule and vagina is eliminated. This is particularly advantageous in obstetric patients when a "clean" urine specimen is desired within a few days postpartum, since contamination by the lochia can be entirely avoided. Such specimens should show approximately the same findings as a catheterized specimen with the advantage of avoiding actual catheterization and its dangers.

185 NORTH WABASH AVENUE

DIFFUSE SARCOMA OF THE ENDOMETRIUM

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SARCOMA of the myometrium is relatively infrequent since not more than 2 per cent of the fibromyomas of the uterus are true sarcomas. Even less common is sarcoma of the endometrium which occurs in a ratio of 1:6 to sarcomas arising in the myometrium (Meyer¹). This ratio appears to us to be inordinately high as we were unable to find a record of a case of sarcoma of the endometrium in the files of the New York Post-Graduate Hospital. It thus seemed to us that a diffuse sarcoma of the endometrium was sufficiently unusual to be of especial interest.

The endometrial sarcomas are divided grossly into the more frequent circumscribed and the rarer diffuse types. The circumscribed is often polypoid and usually arises in the cervix in young individuals. The case we are reporting is an example of the diffuse type involving the entire endometrium. Sarcomas of the endometrium described by Meyer in Henke and Lubarsch cover the subject to 1930. Since then Ward² (1931), Needles³ (1933), who included a sarcoma similar to the one reported here with three "polymorphous sarcomas," and Offergeld⁴ (1933), have described diffuse endometrial sarcomas. The gross and histologic descriptions in these reports agree with our findings.

The history of our case was as follows:

J. B., white, married, female, fifty-five years old, with two children, twenty-seven and twenty-four years old, respectively, came to the dispensary of the New York Post-Graduate Hospital, April 3, 1933, complaining of frequency of urination for the past year and pain in the lower abdomen and profuse vaginal discharge for the past three months. There had been no loss of weight and no bleeding since the menopause, three years previous to admission.

Physical examination showed a rather stout patient with senile changes of the introitus and vagina, marked erosion of the cervix with profuse mucopurulent discharge. The uterus was retroverted, somewhat enlarged, and fairly hard. The cervix was coagulated with the Cherry bipolar electrode and healed very well but the discharge continued unabated. On May 15 a dilatation and curettage was performed by one of us (Moench) and a large amount of necrotic, friable, foul-smelling material mixed with pus and blood was evacuated from the uterus. The tentative diagnosis was necrotic fibromyoma or sarcoma, or carcinoma. A total hysterectomy was advised. This was done on May 26 (Moench). The cervix was first tightly packed with gauze soaked in iodine, the vagina thoroughly swabbed out with the same agent, and a laparotomy performed. Both adnexa were removed with the uterus. Because of the probability of malignancy no clamps were used on the uterus itself. The bladder was rather firmly attached to the uterus but was freed without mishap.

The patient did extremely well until the evening of the fourth day when she suddenly became cyanotic, with cold extremities, and was bathed in cold sweat. Pulse 110, respiration 30, temperature 101°. Despite all measures the patient died the next day. Although an autopsy was not permitted the cause of death evidently was of an embolic nature.

Pathologic Specimen.—The surgically removed specimen was a uterus (including the cervix and with both tubes and ovaries attached). It was 100 mm. in length and 35 by 40 mm. in diameter at the cervical end, and at the fundus measured approximately 42 by 35 mm. It had been split open disclosing a uterine canal lined by an irregularly thickened endometrium 20 mm. in thickness in some areas. The superficial portions were gray green in color, apparently largely necrotic and infiltrated by purulent exudate. In the deeper portion there was a gray opaque layer



Fig. 1.—Uterus showing (A) diffuse, seminecrotic tumor roughly demarcated from (B) the myometrium. (C) Cross-section of uterine wall: (1) Diffuse thickening of endometrium (2) myometrium.



Fig. 2.—Cross-section of uterine wall (low power). A, Diffuse sarcoma of endometrium (no endometrial glands). B, Myometrium.

about 5 mm. in thickness which poorly demarcated the involved endometrium from the underlying myometrium. The serosal surface was smooth and the tubes and ovaries were without gross pathology. Besides the uterus itself (Fig. 1) there were also several pieces of partly necrotic grayish tissue apparently from the interior of the uterus, the largest measuring 35 by 25 by 22 mm. Sections extending through the ragged lining of the uterine canal and myometrium (Fig. 2) show the following microscopic pathology:

There is a lining of necrotic tissue and purulent exudate beneath which there is viable neoplastic tissue (Fig. 2, *A*). The neoplastic tissue is formed by an edematous diffuse proliferation of somewhat irregular cells with large deep-staining nuclei and very abundant mitotic figures (Fig. 4). The cells which often form poorly defined irregular nests are in some places spindle-shaped and in other places present multiple branches which extend to the neighboring cells. When stained by van Gieson's or Mallory's connective tissue method, it is possible to recognize connective tissue fibrils running through and between these cells, indicating their origin from connec-

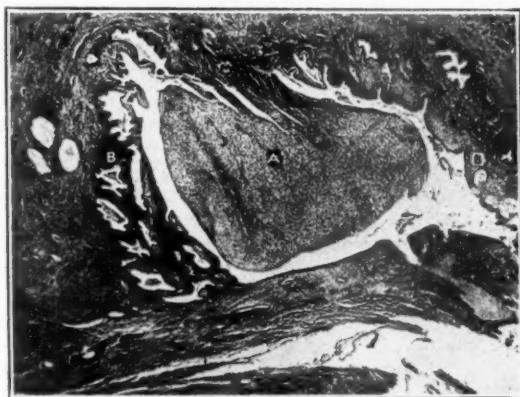


Fig. 3.—Section from cervical region (low power). *A*, Polyp of tumor projecting into dilated cervical gland. *B*, Cervical mucosa with normal glands.

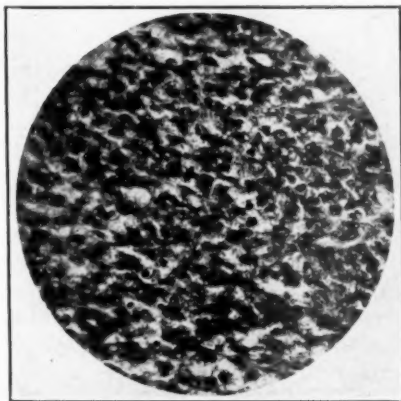


Fig. 4.—Endometrial growth (high power). Diffuse sarcoma cells of endometrium. Note relation to reticular fibers and the numerous mitoses.

tive tissue rather than from epithelium. There are no endometrial glands at any point and epithelial cells are not recognized. At the point of transition to the cervix the sarcomatous proliferation ends except for occasional extensions into the cervical gland ducts (Fig. 3). In some areas the neoplastic cells extend between the adjacent muscle bundles in the myometrium, and the deeper portions of the myometrium contain numerous collections of lymphocytes. *Diagnosis:* Diffuse sarcoma of the endometrium.

Meyer considers that all the variations of endometrial sarcoma are of one cell type derived from the endometrial stroma.

The diffuse sarcomas of the endometrium are usually divided into the following types: namely, those with (1) large round and spindle cells, (2) decidua-like cells, (3) giant cells with small round and spindle cells, and (4) small round cells (Ruge).

The manner of diffuse growth and the type of the neoplastic cells in our case warrant a diagnosis of diffuse round and spindle-cell sarcoma arising from the connective tissue of the endometrium.

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Superbi, Carlo: Echinococcic Cyst of the Liver During Pregnancy, Clin. obstet. p. 639, 1935.

The author describes a case of suppurative echinococcus cyst of the liver which was mistaken for an ovarian cyst and discusses the symptomatology of pregnancy complicated by echinococcus cyst. After eleven hours of labor of this primigravida, a midwife discovered the presence of a complicating abdominal tumor. The author, immediately summoned, excluded twin pregnancy and ascertained a cystic tumor apart from the pregnant uterus. The patient was spontaneously delivered of a live child. She reacted normally, had no rise of temperature during the puerperium and entered the hospital forty days postpartum for removal of the cyst. At that time the abdominal mass, smooth surfaced and movable, slightly deviated to the right, reached three fingers above the umbilicus. Normal sized uterus, anteverted, movable, was palpated to be not connected with the mass. At laparotomy tumor was found to be attached to right lobe of liver with dense adhesions to liver, gallbladder and omentum and was removed with difficulty. Abdomen was closed with opening left for drains. With rise of temperature on seventh day pleuritic exudate developed. Purulent fluid was removed twice, 150 and 170 c.c., respectively. Finally rib resection was done resulting in perfect recovery. A few months later patient again became pregnant and later gave birth to a full-term baby.

The removed cyst weighed 3,600 gm. and consisted of two parts, the one the size of an orange, the other the size of a seven months' pregnant uterus. They contained a purulent, yellowish fluid with many echinococcic cysts.

Failure of proper diagnosis is excusable in the face of the assertion of many writers (Mangiagalli, Boursier, Abadie and others) that differential diagnosis between echinococcic and ovarian cysts is difficult. Franta (1902) collected from the literature 51 cases in which the first symptoms of echinococcus appeared during pregnancy, and 40 instances in which they were discovered during the puerperium. Some writers (Alfieri, Bertino and Alamanni) recorded their rapid growth during pregnancy. In the opinion of Franta, pregnancy favors not only growth but also suppuration of these cysts. As shown in Superbi's own case, the complicating echinococcic cyst may not interfere with pregnancy, labor or development of the fetus. When located in the pelvis, the cyst may cause abortion and more often becomes responsible for dystocias endangering the life of the fetus.

AUGUST F. DARO.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

THE EVALUATION OF PRENATAL CARE*

IN VIEW of the increasing interest in maternal morbidity and mortality and the emphasis placed on prenatal care by physicians and administrative groups in general and obstetricians in particular, the recent report by Drs. Tyler, Watkins, and Walker is particularly significant. Their study is an attempt to evaluate quantity and quality of prenatal care. The specific question for which the answer was sought is stated thus: "If all other contingent factors are the same, what, if any, is the effect on the survival of the mother of various services described as prenatal care?"

Under careful supervision the records of 285 ward deliveries taking place in the New Haven Hospital, and 930 ward and out-patient delivery records of the Boston Lying-In Hospital were subjected to very careful scrutiny and statistical juggling.

Elaborate four-page record forms for compilation of data were used. From data so obtained patients were grouped accordingly as they received adequate or inadequate prenatal care. It is pointed out that the term "inadequate care" rather than "no care" was used because so few patients can be found among deliveries of a high grade maternity service who have had no prenatal care.

After careful grouping according to quantitative standards of prenatal care received, the groups thus resulting were balanced with reference to age, parity, plurality, legitimacy, color, race, economic status, and time of year. Comparison was thus secured at the expense of decided diminution in group numbers, serious but perhaps unavoidable objection to the study.

The balanced groups thus obtained were then subjected to searching analysis of complications of pregnancy and labor and the outcome of delivery. "The groups were found to be strongly influenced in the first outcome by a lack of balance revealed in complications of pregnancy. Apparently, women who have knowledge of some previous impending complication bestir themselves to obtain considerable care and attention. Conversely, those who have gone through former pregnancies without difficulty, or have otherwise found no reason for fear, appear often to neglect proper prenatal care, and will accordingly be classed in the B or intermediate group." (A, adequate prenatal care. B, inadequate and C, intermediate.) "To adjust for this a final balancing of the A and B groups with respect to complications of pregnancy was carried out with the large Boston case series. The excess of each complication (in one group or the other) was removed through random withdrawal by lot from all those who had that particular complication. A final recheck of age, parity and the like was then made to insure that balance of those factors had not been unduly disturbed. The end result was the formation of two comparable groups (A and B) differing only in the degree of prenatal care received, in which groups the course of labor and the final outcome could be studied."

*Report on the Evaluation of Prenatal Care, by Drs. Tyler, Watkins and Walker, Yale University School of Medicine. Published by the Institute of Human Relations, New Haven, Conn., 1934.

The report is interesting, timely and significant. It is well written and apparently fulfills necessary statistical requirements. From data obtained the authors draw certain conclusions, most significant of which is their failure to demonstrate benefits of prenatal care. While the conclusions drawn are doubtless tenable on the basis of data studied, I cannot believe it correctly evaluates prenatal care. In the first place, the study is a comparison of groups receiving prenatal care and frequency or number of prenatal visits is not always a safe index to its quality. Second, whether the number of records studied is adequate may be seriously questioned. The benefits accruing to patients from prenatal care can be ascertained only by comparing with large groups not so fortunately cared for. Furthermore, many complications of pregnancy are uncommon and no satisfactory evaluation of prenatal care in these cases can be hoped for except through analysis of very large groups. It is unfortunate that the basis for comparison in the series studied was not more satisfactory. The doubt and misunderstanding engendered by this report may delay but will not prevent a healthy development of prenatal care.

That prenatal care fails to accomplish a marked reduction in the number of complications at the time of delivery, is not surprising. In general with the exception of deformities, toxemias, and complications arising from coexisting disease (tuberculosis, nephritis, heart disease, etc.), most delivery complications cannot be foreseen. Recognition of abnormalities during pregnancy does not necessarily minimize the problems to be faced at the time of delivery. Knowledge of these threatening potentialities is nevertheless worth while even though we cannot always use it to advantage—an indication, perhaps, of shortcomings in the management of labor rather than futility of prenatal care. Such complications as placenta previa and premature separation are not prevented by prenatal care, but such care is likely to render patients more awake to untoward symptoms and therefore lead to earlier application of remedial measures.

If prenatal visits do no more than give the patient confidence and moral support during pregnancy such care still would be worth the effort. It does much more than this, however, for as pointed out in the preface to this report, “. . . experience of hospital and home delivery maternity services in England and in this country is quite uniform to the effect that maternal mortality, the incidence of stillbirths, and the neonatal mortality are lower when the expectant mother has had appropriate prenatal supervision, at least during the last three months of pregnancy, than is the case when women of similar parity, age, race, and economic status; and with comparable obstetric and aftercare, are delivered without having had the benefit of the medical and nursing supervision. In such conditions as syphilis in the expectant mother and in women with contracted or deformed pelves, the value of prenatal medical examination is so great as to be beyond dispute.” The many intangible benefits which accrue to patients from adequate prenatal care are probably not accessible for statistical measurement. Prenatal care has not been overemphasized, but there is abundant evidence to show that care at the time of delivery and thereafter has been greatly underemphasized.

A pertinent point brought out in this study is that: “Negative prenatal care benefits throughout our several projects have been interpreted as substantiating the growing feeling that obstetric care at labor may play by far the greatest rôle in improvement of maternity outcome. If this be true, prenatal care can render a signal service by directing pregnant women to make arrangements for a high quality delivery service.”

No amount of prenatal care can compensate for poor care at the time of delivery, but good care at the time of delivery can often compensate for lack of prenatal care and can be the most potent single factor for good or bad obstetrics.

—Norman F. Miller, M.D.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK

Review of New Books

Endocrinology

The second edition of *Recent Advances in Endocrinology*¹ by Cameron differs from most of the books on the subject, in that it stresses the fact that endocrinology is "essentially a biochemical subject." Written by a biochemist, on the very first page of the introduction the author emphasizes a statement, the truth of which I have for many years tried in vain to sell to the profession, namely, that a given gland may produce "too much or too little of these specific compounds but it does not produce abnormal compounds."

This book, from cover to cover, is replete with accurate information, particular emphasis being laid upon the biochemic phases of endocrinology. It is surprising that a biochemist has been able to summarize the clinical aspects with such clearness and decisiveness. Occasionally while trenching upon therapy he has been slightly misled but not to anything like the same degree noted in most books on this subject.

The literary references are also extremely well chosen and cover the subject up to August, 1934.

All in all this is a most exceptional and valuable book which can be studied with equal profit by the practitioner, the specialist, and the experimentalist in this subject.

—R. T. Frank

The second edition of *Hormone und Innere Sekretion*² appears six and a half years after the first. Some six thousand new publications have been incorporated, which has almost doubled the size of the book. This is the summary of endocrinology covering general endocrinology, pancreas, thyroid, parathyroid, adrenal, hypophysis, the gonads, as well as other glands without external ducts which have been considered as possible sources of internal secretions. To some extent it resembles our physiologic reviews, except that the entire field has been covered in 368 pages. As most of the references have been taken from abstracts, a large number of minor errors have crept in which, however, are largely compensated for by the fact that the author has a wide and deep acquaintance with endocrinology.

This epitome will be found of great use in locating references or rapidly surveying the field of endocrinology, as it is well arranged and each chapter is followed by a fairly full bibliography.

—R. T. Frank

¹*Recent Advances in Endocrinology*. By A. T. Cameron, Ed. 2, with 55 figures, including 2 plates, and 406 pages. P. Blakiston's Son & Co., Philadelphia, 1935.

²*Hormone und Innere Sekretion*. Von Dr. Fritz Laqueur, Professor an der Universität Frankfurt. Zweite, verbesserte und bedeutend erweiterte Auflage. Verlag von Theodor Steinkopff. Dresden, 1934.

Harrow and Sherwin have attempted the difficult task of making the *Chemistry of the Hormones*³ accessible to the medical profession. The text is so well arranged and so simplified, as well as supplied with chemical formulas, that even the physician who has not kept up with modern organic chemistry can obtain much knowledge from its pages. The authors have taken up the various hormones, some of which, like the thyroid, the adrenal medullary, the male and female sex hormones, have been isolated. Such properties as are known of the less well isolated hormones are likewise described. It contains an enormous fund of information. As the advances in this field are so rapid, it will require frequent revision. For example, since its publication in April, 1934, the chemical and structural formula of progesterin as well as its synthesis from the soya bean have been developed, which, of course, could not be incorporated in this valuable monograph.

—R. T. Frank

Goldzieher's *Practical Endocrinology*⁴ is designed as a guide to the general practitioner, particularly to help him interpret symptoms and to "direct his attention to the culprit gland." In its preface the author emphasizes that he is largely influenced by the pioneer work of Allen Winter Rowe.

The introductory chapters on the morphology and physiology of the glands are purposely short and clear. The chapter on examination of the endocrine patient gives an excellent résumé of the various biologic and pharmacologic tests which will be found useful to the general practitioner for understanding the rationale and purpose of these tests. The description of the symptomatology, on the whole, bears careful scrutiny.

The same cannot be said for the therapy, which, on the whole, is much more optimistic than the reviewer feels warranted, as he does not have the same confidence in diagnosis or the efficacy of the drugs and products recommended. This book compares favorably with a large number of similar volumes which are appearing at the present time. Its chief merit lies in the fact that the author has a wide experience in endocrinology which he has presented in an understandable fashion.

—R. T. Frank

Another approach to the study of cancer is offered in da Costa's monograph *The Action of Hypoglycemic Substances Upon Certain Fermentative Processes of Neoplastic Tissue*⁵ which forms one issue of the "Arquivo de Patologia," published by the Portuguese Institute for the Study of Cancer. The author has studied both normal and neoplastic tissues in both human beings and animals from the chemical, pharmacologic, and therapeutic points of view. He has devoted himself mainly to the effects produced by insulin and allied substances upon those having neoplasms. He finds that insulin injected into animals having neoplasms produces a diminution in the size of the tumors, but not their complete regression; that all tissues, both neoplastic and normal, show a hypoglycemic substance, an "insulinoid," more abundant in the former than the latter; that hyperadrenalinemia and hyperglycemia are produced in animals and in human beings by radiotherapy, and that insulin applied locally to tumor tissue results in a cicatrization and regression of the tumor.

³*The Chemistry of the Hormones*. By Benjamin Harrow, Ph.D., Associate Professor of Chemistry, City College of New York, and Carl P. Sherwin, M.D., of St. Vincent's and French Hospitals. Williams and Wilkins Company, Baltimore, 1934.

⁴*Practical Endocrinology*. By Dr. Max A. Goldzieher, Endocrinologist, Gouverneur Hospital, etc. Illustrated, 326 pages. D. Appleton-Century Co. Inc., New York, 1935.

⁵*Arquivo de Patologia. Orgao do Instituto Portugues Para O Estudo do Cancro*. Publicado por F. Gentil e M. Athias. Vol. VI, No. 2, Agosto, 1934. Palhava, Lisboa.

There are also numerous studies on the effects of radiotherapy and the action of insulin upon the tissues so treated.

The work is painstaking and thorough, and the literature has been completely covered. It should prove invaluable to those working along cancer lines.

—Frank Spielman

Obstetrics

In these days of frequent cesarean sections it is refreshing to find a book on operative obstetrics which stresses delivery from below. DeCamargo's *Manobras e Operacoes Obstetricas*,⁶ with a foreword by Magalhaes, is to be praised if only for this reason. The different maneuvers which can be utilized in vaginal delivery are clearly, concisely, and intelligently presented. It is astounding to ponder upon the enormous number of methods in use. Nor is abdominal cesarean section neglected. The work, however, is an excellent testimonial to the fact that operative obstetrics can be taught and learned, but that obstetrics must remain an art in which the judgment of the individual in the choice of maneuver or operation is of prime importance.

It may be suggested to the author that his extensive bibliography, evidence of considerable effort, can stand revising. Many inaccuracies as well as mistakes in spelling are found here. His illustrations although adequate may also be improved. On the whole, in the field of operative obstetrics the book covers the ground thoroughly.

—Frank Spielman

Short concise texts in medicine may be exceedingly useful. The average monograph, whether published in book form or as a long article, serves as an example. Of course, in this type of work the author almost invariably limits himself to one particular phase of a subject and usually treats it exhaustively. On the other hand, attempts are repeatedly being made to boil down entire medical specialties within the covers of books two or three hundred pages long. The following two books, little more than pamphlets, fall within this category, and are therefore reviewed together.

Devraigne, as part of a "medical introduction" series, contributes two short books on obstetrics, viz. *Propédeutique Obstétricale*,⁷ and *La Pratique Obstétricale*.⁷ The former consists of seven short chapters dealing with fecundation, development of the fetus, examination of the patient, normal delivery, and the normal presentations. The latter discusses briefly infectious diseases, toxemias, gastrointestinal conditions, blood and urinary abnormalities, and affections of the nervous system associated with pregnancy. There are also uterine anomalies, abnormalities of the uterine muscle, of the soft parts, and of the pelvic girdle. Operative obstetrics is covered in very few pages. Taken together, these two books give the impression of disconnected, disjointed material hastily got together for publication. They are neither fish nor fowl nor good old-fashioned obstetrical primers.

—Frank Spielman

⁶*Manobras e Operacoes Obstetricas*, pelo Docente Dr. Joao Pereira de Camargo, Livro Docente da Faculdade de Medicina da Universidade do Rio de Janeiro, etc. Segunda edicao correcta e augmentada, contendo 15 trichromias, 242 clichés e 4 microphotographias. 498 pages. Livraria Francisco Alves, Rio de Janeiro, 1935.

⁷*Propédeutique Obstétricale*. Par L. Devraigne, accoucheur de Lariboisière. 191 pages. Masson et Cie, éditeurs. Paris, 1934.

La Pratique Obstétricale. Par L. Devraigne, accoucheur de Lariboisière. 244 pages. Masson et Cie, éditeurs, Paris, 1935.

This little volume, entitled *Aid to Obstetrics*,⁸ as a matter of fact is designed as an aid to students preparing for an examination in obstetrics. For this purpose it is well adapted, since it brings in succinct form all essential facts, including indications and details of technic of most obstetric operations. Its appearance in a tenth edition must be accepted as proof for its usefulness and popularity.

—Hugo Ehrenfest

Among the diseases encountered as complications of pregnancy, *Pulmonary Tuberculosis*⁹ holds first place both in regard to frequency and practical importance. Though an enormous literature has accumulated, the question of the effects of disease and pregnancy on each other has remained unsolved. In marked distinction to many previous contributions in this monograph the exact histories are presented of 360 pregnancies observed in 215 tuberculous women. Diagrammatic sketches, x-ray plates and graphic charts establish for almost every case not only actual conditions but as well the changes noted in the course of many years. Critical analysis of the case records and appropriate tabulations from various viewpoints permit clear insight into the life histories of all these patients. From them the author draws his conclusions which start with the significant statement: "The problem of pregnancy in the tuberculous woman is not solved." In his opinion, it is possible to determine with some certainty for some patients the probability of acute and even dangerous aggravation of her disease, but this unfortunate effect certainly is rarer than commonly believed. There are means available to protect the woman against such a deleterious effect. No definite rules can be established for advisability or necessity of interruption of pregnancy.

Though the writer's views, especially in regard to contraception, sterilization and even interruption, are clearly and inevitably influenced by laws and public opinion at present prevailing in Germany, the monograph proves of unusual interest and value particularly through its careful presentation and critical analysis of the large material.

—Hugo Ehrenfest

This small monograph¹⁰ deals with the *Unexpected, Sudden Death of the Patient During Pregnancy, Labor, and Puerperium*. It consists of a thorough review of all reported cases in which sudden death was due chiefly to a great variety of complicating and often unsuspected diseases and anomalies.

—Hugo Ehrenfest

This historical volume¹¹ includes 15 communications of various authors, dating from 1770 to 1831, on the subject of *Symphyseotomy*.

It is gotten up in a faultless fashion with a number of portraits and illustrations. The material was collected and edited by *Nederlandsch Tijdschrift voor Geneeskunde*. It should prove of great interest to those interested in the history of medicine, particularly those who read the Dutch language.

—R. T. Frank

⁸*Aids to Obstetrics*. By Leslie Williams, Obstetric Surgeon to Out-Patients, St. Mary Hospital, London, etc. Tenth edition. William Wood & Co., Baltimore, 1934.

⁹*Lungentuberkulose und Schwangerschaft*. Von H. Braeuning, Chefarzt der Fues-sorgenstelle fuer Lungenkranke in Stettin, etc. 275 pages. Mit 391 Kurven und Abbildungen. Verlag von Georg Thieme, Leipzig, 1935.

¹⁰*Der Unvermutet Schnelle Tod in Schwangerschaft, Geburt und Wochenbett*. Von Geh. Med. Rat Professor Dr. Erwin Kehr, Direktor der Univ. Frauenklinik in Marburg. 52 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

¹¹*Opuscula Selecta Neerlandicorum de Arte Medica*. Varii auctores se symphy-siotomia. Aangeboden door het Nederlandsch Tijdschrift voor Geneeskunde, 1934.

This report on the *Evaluation of Prenatal Care*¹² is the subject of a special communication by Prof. Norman Miller in this issue of the JOURNAL.

—R. T. Frank

This monograph, on *The Conception Period of Women*,¹³ translated from the Japanese and published in the United States, gives a summary of Ogino's views. His personal observations are based on 132 laparotomies in which the time of the menstrual cycle was compared with the ovarian findings. He also has a moderate number of personal observations on the time of conception and the time of so-called functional sterility in the cycle.

Ogino reviews both the provoked ovulation theory as well as the effect of cyclical trauma. In regard to the latter he has convincing evidence obtained after the earthquake of 1923. In the month succeeding the catastrophe, he obtained the menstrual cycles of over 200 high school pupils in the affected area and compared it with a similar group in an area not involved, without finding any change.

According to Ogino, the sterility phase begins twenty-four hours after ovulation. Sperma, he claims, is at most able to fertilize for three days.

This brief monograph is of great interest as it summarizes the world's literature in an excellent fashion and gives a clear-cut outline of the author's personal views. However, I feel that the material is far too scant as yet to permit us to consider the Ogino-Knaus hypothesis definitely proved.

—R. T. Frank

This report on *Maternal Mortality in Philadelphia*¹⁴ contains a wealth of statistical material which appears to have been carefully collected and thoroughly and impartially digested. The problem of maternal deaths in Philadelphia, according to the committee, is fourfold, namely (1) self-induced and criminal abortions; (2) errors in judgment on the part of the medical profession; (3) lack of appreciation of the need of prenatal care by the laity; (4) failure of hospitals, organized medicine and allied agencies to grasp fully their responsibilities and opportunities.

The committee finds that the largest proportion of deaths from criminal abortion is among married women, many of whom having living children. The committee, although not unanimous, appears to favor the advisability of legalization of abortion with proper reservations. In Philadelphia the midwife is almost a negligible factor in connection with mortality, particularly as she is so closely supervised and her activities regulated. The laity is responsible in many cases through ignorance and lack of cooperation in causing preventable deaths. The report appears to be direct, straightforward, and with every effort to favor improvement in order to safeguard the obstetric patient.

—R. T. Frank

The *Elements of Experimental Embryology*¹⁵ deals with the embryology of the prefunctional period mainly. It contains an amazing and bewildering mass of facts and ingenuity of experimentation by means of which some of the basic life processes

¹²*Report on the Evaluation of Prenatal Care.* By Margaret Tyler, J. H. Watkins, and H. H. Walker. A Report to the Sub-Committee on Evaluation of the Committee on Administrative Practice, American Public Health Association. 68 pages. Institute of Human Relations, Yale University, 1934.

¹³*Conception Period of Women.* By Dr. Kyusaku Ogino. English Translation by Dr. Yonez Miyagawa. Medical Arts Publishing Co., Harrisburg, Pa., 1934.

¹⁴*Maternal Mortality in Philadelphia, 1931 to 1933.* Report of the Committee on Maternal Welfare, Philip F. Williams, M.D., Chairman, Philadelphia County Medical Society, 1934.

¹⁵*Elements of Experimental Embryology.* By Julian S. Huxley and G. R. de Beer. With 221 illustrations and 514 pages. Cambridge University Press—Macmillan Co., New York, 1934.

have been analyzed. In differentiation it is immaterial whether a given nucleus finds a given cell. Up to a certain stage in gastrulation the fates of most regions are not irrevocably determined, as shown by transplantation experiments, except in the case of the chorda mesoderm.

Polarity and bilateral symmetry, however, are fixed. The axis of polarity is determined outside of the egg by such influences as light and chemicals. The plane of bilateral symmetry in the frog, for example, is determined by the point of entry of the sperm. All vertebrates are in reality asymmetrical.

Cleavage has little importance in differentiation. The egg of a fly, for example, cleaves only when the multiple nuclei finally reach the periphery. Until then, the cytoplasm is undivided. The dorsal lip of the gastropore in the lower forms acts as an organizer, a formative stimulus which brings about determination of the tissues. Its effect basically must result from chemical influences as the organizer tissue acts when dead and extracts of the organizer tissue likewise act. The composition is probably lipoidal.

Of great interest to the gynecologist and obstetrician is the section devoted to the gonads and sex differentiation. None of the evidence presented settles finally the controversy as to whether the primordial germ cells arise in the special gonad-field or come from elsewhere in the ovum. The authors consider the evidence conclusive that the indifferent gonad-rudiment is normally dependent on its genetic sex constitution although this can readily be overridden by other agencies. The gonad-field has one of two potentialities according to the sex chromosomes which it contains. The primordial germ cells appear to be completely bipotential as regards sex. The final determination depends on local influences. In the cortex they become female; in the medulla, male. Locally, temperature likewise plays a big rôle.

A considerable portion of the book is devoted to fields and gradients. The appendix is devoted mainly to a new type of experimentation devised by Holtfreter, based on the discovery that removing the membranes from the early blastulae of axolotls and then placing the tissues in Ringer's solution causes eversion of the layers or so-called exogastrulation and separation of the ectoderm with all of its resultant nervous tissue from the endomesoderm.

This book will prove most fascinating to any reader who is interested in the fundamental problems of biology.

—R. T. Frank

Introduzione allo Studio Dell' Eugènica,¹⁶ by Cristalli, is obviously designed for the novice as an approach to the study of eugenics. The commonly accepted views are presented with adequate illustrations and ample references to the literature. Appended is a glossary of terms peculiar to this field. The material is elementary.

—Frank Spielman

Dr. J. Morris Slemons has written *A Handbook for Women During Pregnancy*.¹⁷ It begins with the signs of pregnancy and the date of confinement, and covers embryology, prenatal care, labor, puerperium, and the lactation period. Written by an experienced obstetrician, it doubtless will find its field and circle of readers.

—R. T. Frank

¹⁶*Introduzione allo Studio Dell' Eugènica* (Eredita biologica). Par Prof. Giuseppe Cristalli. Stabilimento Industrie Editoriali Meridionali, Napoli, 1934.

¹⁷*The Prospective Mother*. A handbook for women during pregnancy. By J. Morris Slemons, M.D. Third edition. D. Appleton-Century Co., Inc., New York, 1934.

It is interesting to note that essential instruction can be provided for expectant mothers and prospective fathers also in a (more or less) humorous form. *The Stork Joins the Blue Eagle*¹⁸ is an amusing little volume, in spots (e.g., the chapter entitled: Obstetrical Ward), really funny. As a whole, the author presents only facts which are generally accepted, and recognized as important for up-to-date obstetric care, though we do, incidentally, not share his belief in the practical value of a urinary test for the purpose of determining the sex of the fetus. The Pipe Dream, in the last chapter, picturing the future work of the obstetrician under an NRA code, was interrupted a bit too early by that ringing phone. We had expected that such a code would as well decree a definite shortening of the hours of labor. A provision of that sort, unlike any other existing code, would be heartily approved by both the employer and employee. (This review was written before the Supreme Court decision.)

Every obstetrician should try to keep this little book in his waiting room and, since this probably will not be possible, might preferably induce every pregnant patient to acquire a copy.

—Hugo Ehrenfest

Dr. Kenyon's book on *Healthy Babies*¹⁹ is designed for the expectant mother or the mother of a young child. She therefore devotes chapters to prenatal care and the baby at birth, as well as carrying the child through the third year of infancy. I am sure that many mothers will turn to its pages for help and doubtless and as usual, will here and there be misled when they try to be the child's own physician.

—R. T. Frank

Diseases of Children,²⁰ the standard of its kind in England for a number of years, is now in its third edition. New chapters have been added on blood transfusion, heredity, orthodontia, the newly born infant, diseases of the accessory nasal sinuses and ear, the lipoidoses, acetonemia, cystoscopy and pyclography, rheumatism, allergy, and tuberculosis. Despite the rather formidable number of authors whose names appear on the title page, this by no means completes the list, other writers, thirty-six in all, contributing special articles throughout the work. Naturally, some of these will appeal to the reader more than others, but the treatment of the subject matter is so different from what we are accustomed to in this country, that there are very few chapters which will not have a definite appeal to the American reader. The chapters on functional and organic diseases of the nervous system, diseases of the muscles, and rheumatism were especially fascinating to this reviewer. Happily, the gap which has long existed between the English and American views on the nutritional disorders has been very much narrowed in this edition of the work, a fact which adds to its value as a reference work in this country. In fine, it would seem that no pediatrician who wishes to keep up with the advancement of pediatric thought can afford to be without this book, and even the physician whose interest in the diseases of childhood is a more casual one will soon find that the money spent for this volume is one of the best investments in his medical library.

—T. C. Hempelmann

¹⁸*The Stork Joins the Blue Eagle*. By Fred'k M. Margaretten, M.D. Illustrations by George S. Jacobs. Wamba Printery, Brooklyn, N. Y., 1934.

¹⁹*Healthy Babies and Happy Babies*. By Josephine Hemenway Kenyon, M.D. Little, Brown, and Company, Boston, 1934.

²⁰*Diseases of Children*. Third edition with contributions of thirty-six authors edited by Hugh Thursfield, physician, Hospital for Sick Children, etc. and Donald Paterson, Physician to Out-Patients, Hospital for Sick Children, etc. William Wood and Company, Baltimore, 1934.

Zahorsky's *Synopsis of Pediatrics*,²¹ as the title frankly states, is really a "synopsis." The author emphasizes that he "has tried to cover the essential points in symptomatology, diagnosis, and treatment," and in this he has succeeded admirably. As is to be expected the print is small, the illustrations are few, and the subject matter is treated in short paragraphs composed of short sentences. One experiences a feeling of haste while reading it.

—Frank Spielman

Gynecology

The second half of the sixth volume of Stoeckel's *Handbuch der Gynäkologie*²² is devoted to the clinic of uterine tumors. This is a huge contribution, 838 pages in length and costing 148 R.M.

It is somewhat unequally divided but covers a tremendous ground. The late v. Peham deals with the etiology, symptomatology, and treatment of uterine myomata in 181 pages.

P. Esch described uterine sarcomata in 31 pages. H. Martius covers radiotherapy of uterine myomata and sarcomata in 185 pages. O. Pankow devotes 400 pages to the therapy of uterine carcinoma and chorionepithelioma, including a shorter contribution of Schönholz on chemotherapy of cancer.

Peham in his description of myomata, contributes nothing new to the etiology. In 1,878 fibroids, carcinoma was found in 3.8 per cent (corporeal 0.53 per cent, cervical 3.3 per cent). He found no excess of corporeal carcinoma. Sarcoma was noted in only 2.78 per cent. He believes that the symptoms following castration are greater than those following hysterectomy.

Esch finds that there is 1 sarcoma to 28 carcinomata of the uterus. In 2,914 cases of uterine neoplasia, 1.3 per cent was sarcoma.

Martius believes that the roentgen effect on myomata is purely through the ovaries. He believes that treatment can be graduated so as not to destroy completely the ovarian function, but merely to bring about an "exovulation." He likewise considers the symptoms following hysterectomy less marked than following x-ray treatment. He found no increase of carcinoma after radiotherapy of myomata. He is strongly opposed to temporary sterilization as he believes that it has a bad effect on subsequent pregnancies, nor is he in favor of preputiary and splenic radiation. He likewise deals with the radiotherapy of sarcomata. The effect of radium in the uterus he considers more upon the mucosa but likewise affecting the ovaries. His descriptions of technic are sufficiently detailed to interest the radiotherapist, but likewise understandable to the gynecologist who has not equipped himself especially in this branch.

Pankow describes in utmost detail the operations for uterine carcinoma both from above and below. Likewise the radiotherapeutic treatments and combinations of operation and radiotherapy. The statistics and literature dealing with operability and mortality, and final results are given in great detail. He believes that the preference as to operation or radiation and operation is by no means settled. In the treatment of corpus carcinoma he advises to start the operation abdominally in order to remove the glands and then, depending upon individual preference, experience or the type of case encountered, to finish by a complete hysterectomy either through the abdomen or by the vaginal route.

²¹*Synopsis of Pediatrics*. By Dr. John Zahorsky, professor of pediatrics, St. Louis University Medical School, etc. With 77 illustrations in the text and 6 color plates, 349 pages. The C. V. Mosby Co., St. Louis, 1934.

²²*Stoeckel's Handbuch der Gynäkologie*. Sechster Band, zweite Hälfte. Die Klinik der uterus Tumoren bearbeitet von Esch, Martius, Pankow, Peham und Schönholz. Mit 160 zum Teil farbigen Abbildungen im Text. 838 pages. Verlag von J. F. Bergmann, Muenchen, 1934.

Schönholz's chapter on chemotherapy gives a very excellent review of the literature. The author concludes that at present we are not yet justified to treat carcinoma solely by chemical means.

The 160 illustrations in the text are mainly from standard sources such as Peham-Amreich: *Gynecological Operations*; Schauta, Stoeckel, Wertheim, Franz, etc.

This volume is of particular value to the clinician as it enables him to find the references to original sources collected in a conscientious fashion.

—R. T. Frank

Meigs's *Tumors of the Female Pelvic Organs*²³ is largely a personal book and is in the main based on a series of cases which the author studied from the Massachusetts General Hospital. Its appeal should be mainly to the general surgeon who does gynecologic work, although the gynecologist, pathologist, and roentgenologist may find matters of interest within its pages.

More than one-fifth of the book is devoted to carcinoma of the cervix. In 45,503 admissions to the Massachusetts General Hospital, among married patients, over thirty years of age, 1.6 per cent showed carcinoma of the cervix. The author appears a disciple of the chronic irritation theory as the causation for cervical cancer. However, he emphasizes that repair of lacerations, as shown by Woolston's series, did not reduce the incidence of the disease. He recognizes that biopsy material produces many inaccuracies of grading, but believes that examination of the entire uterus with grading in mind, is of value. Of the 110 cases at the Massachusetts General Hospital, one-half of the patients were operated upon and one-half were treated by radiation. In the 13 cases of stump carcinoma, Meigs considers the prognosis poor. This is contrary to my personal observations.

In many of the conditions the series of cases are too small to make the statistics of value. In fibroids of the uterus, 44 cases or 0.6 per cent showed malignant changes, again contrary to my observations. He considers x-ray even of less use than radium. In our experience sarcomata have been extremely radiosensitive.

The classification of ovarian tumors is based on 327 cases, including 100 simple cysts. It appears that there is much reduplication in the classification adopted by Meigs, although it does not differ greatly from the accepted classifications.

The chapter on metastases is of exceptional value.

The gross illustrations of the book unfortunately have been reduced too greatly, thus obliterating to a large extent their excellence. The photomicrographs are good and valuable throughout.

Although considerable literature is mentioned at the end of the chapter, the bibliographies are not sufficiently complete to permit of using the volume as a book of reference. The text is simple, clear, and easily read.

—R. T. Frank

This compact enumeration and description of all the actual and possible *Effects of an Accident on the Female Genitalia*,²⁴ as recorded in literature, evidently has been prepared for the benefit of gynecologists, appearing as medical experts in German courts. They must possess and prove thorough familiarity with this complex problem. The small monograph deals in great detail with actual injuries and with possible relations of trauma to alterations in position and function of the nonpregnant uterus, and with its effects on an existing gynecologic disease or pregnancy. In

²³*Tumors of the Female Pelvic Organs*. By Joe Vincent Meigs, Instructor in Surgery, Harvard Medical School, etc. With 261 illustrations. The Macmillan Company, New York, 1934.

²⁴*Weibliche Geschlechtsorgane und Unfall*. Von Professor Dr. August Mayer, Direktor der Univ. Frauenklinik in Tuebingen. 82 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

this latter respect even the influence of an accident on labor through resulting inertia or scar constrictions is considered. The monograph closes with a carefully prepared and classified list of bibliographic references.

—Hugo Ehrenfest

Miscellaneous

This volume,²⁵ entirely free of any chauvinistic motive, attempts simply to show in how far medical men of the Jewish race have helped to bring American medicine to its present high rank. Chapter I briefly surveys earlier history and starts with the interesting statement that Columbus had with him five Jews, two of them being ship's physician and ship's surgeon respectively. There follows the listing of physicians, prominent in the author's judgment, each chapter devoted to a special field of medicine, closing with Chapter XV, in which are given the men who have written on the History of Medicine. One of the several appendices brings the description of all existing Jewish Medical Institutions.

The author prepared this comprehensive work by a personal study of all available medical literature and this fact probably accounts for two minor shortcomings: Some men, well known locally and nationally as outstanding clinicians and skilled operators but not given to writing, have been overlooked, while, on the other hand, the importance of others has become exaggerated through the number of their, often not very important, publications. However, there can be no doubt that this volume represents a very valuable contribution to the history of medicine in this country.

—Hugo Ehrenfest

The second edition of the *Standard Classified Nomenclature of Disease*,²⁶ compiled by the National Conference on Nomenclature of Disease, appears three years after the first. It has been accepted for use in the record rooms by 120 of the large hospitals in the United States and Canada and, as I can say from personal experience, appears in a large measure to solve the problem of classification. Some 2,000 additional items have been added so that at present it covers approximately 15,000.

Although at first sight confusing, the classification in practice works out well. Many omissions have been corrected and debatable points clarified.

It would be advisable for those hospitals which have not accepted the classification, to install it in their record rooms in order that the statistics of the entire profession in the United States be recorded according to the same formula and thus be more readily comparable.

—R. T. Frank

The main object of this book is to outline *Nursing Technique*²⁷ as taught in the Associated Hospitals of the University of Minnesota. The material, as in the previous edition, is arranged in lessons. It should prove of real value to teachers in training schools as well as to nurses preparing for examinations.

—R. T. Frank

²⁵*Jewish Contributions to Medicine in America (1656 to 1934)*. By Solomon R. Kagan, M.D. With medical chronology, bibliography and 69 illustrations. 549 pages. Published by Boston Medical Publishing Co., Boston, 1934.

²⁶*Standard Classified Nomenclature of Disease*. Compiled by the National Conference on Nomenclature of Disease. Edited by H. B. Logle, Executive Secretary. 870 pages. Commonwealth Fund, New York, 1935.

²⁷*Textbook of Nursing Technique*. By Marion L. Vannier, R.N., and Barbara A. Thompson, R.N., Director of the Wisconsin Bureau of Nursing Education, etc. Second edition, revised, 265 pages. University of Minnesota Press, Minneapolis, 1935.

Correspondence

*To the Editor:**

In the *American Journal of Obstetrics and Gynecology* of July, 1934, Dr. Ralph E. Campbell published an article, "The Effects of Chloral Hydrate on the Maternal and Fetal Organism from the Standpoint of Experimental Study." Dr. Campbell introduced into the stomachs of dogs, by means of a tube, 0.4 gm. of chloral hydrate per kilogram of body weight, and then, by very greatly increasing these quantities per kilogram, produced markedly detrimental changes in the liver, kidneys, and heart of these animals. Such results are quite comprehensible. It is acknowledged that chloral hydrate, as well as other powerful drugs, when taken in large doses, is poison to the organism. That is why pharmacologists classify doses as "medical" and "toxic."

Based on his observations on the toxic doses, the author concludes that chloral hydrate should not be used in cases of eclampsia. But this can hardly be regarded as correct. In the first place it is unreasonable to assume that the effect on healthy animals is the same as that on sick ones without definite clinical proof. In the second place, one cannot from the effect of toxic doses predict accurately the effect of medical doses, especially in eclampsia, when ordinarily we employ doses in strength one-tenth or even one-twenty-fifth of those used by Dr. Campbell. It might be more helpful if the author would investigate the influence on dogs of the dosage applied to women with eclampsia. But even then the conclusions could not directly be transferred to the dosage of sick people; healthy animals and sick animals react differently to medical treatment. How much more differently a sick man and a well man.

The experiments in the laboratory of Bezredko in Paris, on animals suffering from anaphylaxis, which has a distinct analogy with eclampsia, have shown that narcotics produced a marked improvement in the state of the experimental animals. The experiments of Anselmino and Hoffman, Küstner and Fauvet with animals injected with hormones from the posterior lobe of the hypophysis have also shown that narcotics have relieved the condition. It is known that these authors suppose eclampsia to be the result of the increased activity of the hypophysis. These authors acknowledged on the grounds of their investigations the prophylactic method to be the rational one. It can easily be explained theoretically. Eclampsia is a toxemia with convulsive attacks. These attacks have a very destructive effect on the organism. The toxemia itself can be fatal to a woman within a couple of months; the convulsive attacks can kill her in a day, sometimes in a few hours. Very strenuous methods are required to stop these attacks, and these measures have been, up to the present, the use of chloroform and chloral hydrate.

I do not wish to imply that it is unnecessary to look for other more effective and safer means to combat eclampsia; many such means have been proposed, including magnesium sulphate, luminal, pernocton, somnifen, avertin, and others. I know, however, that these narcotics in large doses poison the organism, and that with magnesium sulphate some fatalities have occurred. As for chloral hydrate, I do not know of any fatality following upon its use among 2,000 eclamptic patients in

*The publication of Professor Stroganoff's letter was delayed to afford Dr. Campbell an opportunity to make a suitable reply. In view of the association of the former with the well-known conservative method of treating eclampsia, the publication of the original communication and Dr. Campbell's comments should prove of interest to the readers of the JOURNAL.

The Editors.

Leningrad. In short, my principal objection to Dr. Campbell's view is that clinical results must be given first place, and until the superiority of a drug is established clinically, it cannot be recommended for general use, but merely employed for experimental purposes.

Moreover, we cannot renounce the utility of the medicine which has given the best result in fighting a certain illness simply on the basis of experiments upon healthy animals. The best results in the treatment of eclampsia during the last thirty-seven years have been achieved by the prophylactic method; this is acknowledged in the reviews of my published works. For instance, Plass shows that of 5,976 cases of eclampsia treated conservatively only 11.1 per cent were fatal. More than half of these cases were treated by the prophylactic method or its variations. The statistics given in my own work are as follows: of 7,344 cases of eclampsia, treated by the prophylactic method and its variations, 9.7 per cent proved fatal. Of these, 1,400 were treated, with my participation, by the *improved* prophylactic method, and only 6 per cent were fatal. As to the 1,432 children in these cases, 79.7 per cent of them left the hospital alive.

These definite and proved statistics refute entirely the statement of Dr. Campbell about the harmful effects of chloral hydrate in the treatment of eclampsia. As for the measures he recommends, it is my opinion that investigations into the effects of $MgSO_4$, luminal, pernocton, etc., would be valuable, but only if used in conjunction with the prophylactic method which is proved to be sound. Even so, it would be safe to recommend those measures *for general use only on the basis of clinical experiments on two or three hundred cases at the least, and only on the strength of a lower mortality rate in these cases than that which I have quoted above*. I regret that Dr. Campbell gives no statistics about the number of women suffering from eclampsia to whom barbituric acid derivatives have been administered, nor about the results received. I regret also that he does not tell us whether the animals to which these drugs were administered had previously been inoculated with the hormones of the posterior pituitary.

In conclusion I would like to express my opinion that if 1.1, 0.6, or even 0.4 gm. of chloral hydrate per kilogram of weight were introduced into the stomach of any woman with eclampsia, she would die within twenty-four hours.

PROF. W. STROGANOFF.

Leningrad, November 6, 1934.

COMMENT ON THE FOREGOING COMMUNICATION

To the Editor:

Professor W. Stroganoff's criticism of my report on chloral hydrate demands careful consideration.

Litzenberg has pointed out that there are two diametrically opposed groups in the treatment of eclampsia: the radicals who insist on emptying the uterus after the first convulsion, and the conservatives who claim that operative methods are not only unnecessary but actually harmful. Professor Stroganoff belongs to the latter group and his works have been monumental and important in producing a conservative influence.

The criticism of drug dosage in animal experimentation with its application to therapeutics in the human needs no defense. Pharmacology would be at a loss without animal experimentation, as one of its means of investigation. Then, too, pharmacology and toxicology have no fence between them for measuring effects by giving the dose at varying levels. Professor Stroganoff suggests that the dosage

applied to women in eclampsia be tried experimentally in dogs to study the effects. He fails to realize that in animals, to produce a physiologic drug effect comparable to that in the human, entirely different dosages must be used; and sometimes the animal dosage is several times the human dosage. An illustration would be morphine in the dog with its dosage several times that of the human to produce comparable physiologic effects.

Stroganoff points out that experimental conclusions cannot be carried from healthy to sick animals, to say nothing of man. This statement is more academic and theoretic than real. Experimental pharmacology and toxicology would be a great loss to therapeutics if this statement were true.

He reports beneficial results with narcotics in anaphylaxis and makes an analogy in this condition to eclampsia. Several investigators, Johnstone, Murray, Zweifel, Whitridge Williams, and others, have shown negative results; the positive results were attributed to the introduction of the products of placental autolysis; unautolyzed placental tissue gave no reaction. Furthermore, the occurrence of eclampsia with hydatiform mole cannot be explained by the hypotheses which depend on interagglutination or of anaphylaxis.

Professor Stroganoff mentions the observations of Anselmino and Hoffman, Küstner, Fauvet, and others, who attribute eclampsia to the activity of the posterior lobe of the pituitary, and on the grounds of their investigations favor its prophylactic treatment. Harvey Cushing, a noted authority, points out the invasion of the posterior lobe by basophilic cells from the pars intermedia, and other hypertensive states. Byrom and Wilson in most careful and well-controlled experiments were unable to confirm the pressor and antidiuretic effects in several preeclamptic and eclamptic patients as found by Anselmino, Hoffman, and others. Cushing's observation is dependent upon more information concerning the normal limits of basophilic invasion before the evidence is conclusive. Smith and Kunkel are not impressed by the findings mentioned by Cushing; so that in the last analysis Stroganoff is basing his conclusions upon experimental evidence which needs confirmation. DeLee points out that in hundreds of toxemia cases in which posterior pituitary was given during labor that only one woman developed convulsions and that even in this case their causation was very questionable. Schwarz points out that in his large series infundin was given freely without any apparent damage; it would seem once again to indicate that the part the posterior pituitary plays in the etiology of the late toxemias and eclampsia needs definite confirmation. Certainly at the present time no rational conclusion can be drawn in the treatment of eclampsia with pituitary medication.

Stroganoff calls attention to the fact that theoretical deductions are easy in eclampsia—I would say, true enough in most diseases—and he defines eclampsia as a toxemia with convulsions, saying that the latter are injurious to the patient and must be stopped. He states dogmatically that the only means of controlling the eclamptic attack is "up to now" by using chloral hydrate and chloroform. A critical examination of the literature as to the treatment of the eclamptic convulsions shows such contradictory evidence that this statement cannot be accepted. Various agents have been successfully used in controlling the eclamptic convulsions. Mendenhall, Lewis, Bleckwenn, and several others have reported excellent results in the control of the convulsions of eclampsia by sodium amytal. Beck's results in controlling the eclamptic convulsions with huge doses of morphine are convincing. Bleckwenn has had a wide experience with sodium amytal, having given over 2,500 injections to some 200 patients, over a period of a year and a half. One patient alone received over 300 injections during the year; careful studies of elimination in this case failed to reveal any accumulative effect or toxicity. Bleckwenn reported several cases of eclampsia in which the convulsions were readily controlled.

Mendenhall reported in his cases prompt and complete control of the eclamptic convulsions. Lewis' series of cases shows once again that the convulsions can be controlled by sodium amytal. Emge and Hoffman, and Bourne, Bruger, and Dreyer have shown that sodium amytal is not injurious to the liver or kidneys. In these series it has been shown that where morphine and chloral hydrate had failed to control the convulsions, sodium amytal was effective. It is interesting to note that sodium amytal has been just as effective in the control of convulsions of cocaine and strychnine poisoning as in the convulsions of tetanus, meningitis, and rabies. Luminal has been successfully used in the control of the eclamptic seizures by Katsutya, of Japan, who showed a decrease in maternal mortality of 15 per cent by substituting its use for chloral hydrate. DeLee has substituted other drugs for chloral hydrate and chloroform in the treatment of eclampsia. J. W. Harris, of the University of Wisconsin, has removed chloroform and chloral hydrate from his eclampsia treatment and has substituted sodium amytal. Solomons, at the Dublin Rotunda Hospital, has a substitution therapy for chloroform and chloral hydrate, using morphine as a narcotic.

The treatment of eclampsia, a disease of unknown etiology and distinctly empirical as to treatment, must advance with the replacement of old ideas and dogmas, as science offers something better. This does not mean that we should be constantly casting aside methods of treatment one for another; but it does mean that the treatment of eclampsia is so empirical that well-founded and reasonably basic ideas should be considered and perhaps tried in the light of a better treatment, not a new one. Progress in any line of treatment always entails a degree of stability; self-satisfaction with one's method of treatment may be contrary to progress; and inactivity as to the development of newer and better ideas is not synonymous to progress in any line of treatment. Then, too, it is hazardous for one to resign himself to the conclusion that any treatment in medicine is the last word in perfection. It is commendable always to be on the outlook for a better substitution therapy in the furtherance of a cure. A routine treatment may surrender as if nothing requisite is wanting; such a resignation is dangerous and at times precludes advances in treatment; indeed, I am unwilling to admit that Professor Stroganoff has the best treatment for the eclamptic convulsion in the use of chloral hydrate, even though this drug has been used for years and in a great many cases. I am willing to use other drugs which do not have the disadvantages of chloral hydrates and in addition control the convulsions.

The obstetric profession in the United States and in foreign countries should perfect an organization to study comparative values of the different methods of treatment in eclampsia. Directors of large clinics should be willing to adhere to rigid lines of treatment for comparative purposes with other clinics both in this country and abroad; when these procedures are carried out, statistics will then show something of real value for comparison. There is a lack of common terminology; there exist numerous and diversified treatments, and, as Solomons points out, autopsies should be obtained in all deaths to eliminate such errors of diagnosis as brain tumor, cerebral hemorrhage, tuberculous meningitis, syphilis, and other conditions which, at present, are factors of error in statistical mortality rates. Some obstetricians have been unable to approach Stroganoff's results even though adhering rigidly to his treatment. I feel that there is a lack of a common denominator in the classification of cases, interpretations, and methods of treatment.

A common practice in this country is to collect statistics on several hundred cases of eclampsia from numerous clinics and to determine the mortality rate with all kinds of treatment and variations, with a veritable hodgepodge of facts.

I feel certain that, if one of our large obstetric societies would assume responsibility for the study of the eclampsia problem both in the United States and abroad, valuable and useful information would result; and mortality figures would be reasonably dependable. International organization and cooperation could work out as well in eclampsia as it has in cancer. It seems to me that mortality figures as reported by the large clinics in relation to eclampsia should be held with a considerable degree of scepticism and suspicion as to accuracy.

Professor Stroganoff has reported excellent results in the treatment of eclampsia by the prophylactic method and its variations. He appears to conclude from a study of his mortality rate that chloral hydrate cannot be a harmful factor in his treatment. His reasoning seems to be based on the assumption that the mortality rate is the harmful index of chloral hydrate; in other words, the death or survival of the patients. It does not seem to me that the condemnation of a drug is of necessity dependent upon the death of the patient. Obviously many other factors must be considered, as already pointed out in the case of chloral hydrate.

The use of chloral hydrate is dangerous in heart disease in which the heart has already been strained by eclamptic convulsions. Aufrecht has pointed out that the use of chloral hydrate and morphine is particularly dangerous, a combination universally used in the Stroganoff treatment of eclampsia.

Jung has pointed out that large doses of chloral hydrate as used in the Stroganoff treatment may kill the fetus. I have shown experimentally in pregnant dogs that chloral hydrate has produced a deleterious effect upon unborn puppies.

In conclusion, it seems to me that experimental and clinical evidence would strongly justify the exclusion of chloral hydrate in the treatment of eclampsia.

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Item

American Board of Obstetrics and Gynecology

The results of the 1935 examinations given applicants for certification by the American Board of Obstetrics and Gynecology are as follows:

A total of 112 candidates were examined. Of this number, 88 were approved for certification; 22 failed to obtain passing marks (6 of whom were failed and 16 conditioned); and 2 did not complete their examinations.

Below is a list of the candidates approved for certification. These names were announced at the dinner held at the Hotel Traymore, Atlantic City, New Jersey, on June 12, 1935, terminating the Board's two-day examination period.

ALABAMA

DOUGLAS, GILBERT F., Birmingham
GARRISON, JOHN E., Birmingham

CALIFORNIA

KANNER, H. M., Sacramento

CONNECTICUT

PERRINS, HARLAN B., New Haven

DISTRICT OF COLUMBIA

CROWLEY, JEROME F., Washington
DARNER, HENRY L., Washington
NOTES, BERNARD, Washington
ROSS, JULIAN WALDO, Washington

FLORIDA

STRUMPF, IRVING J., Jacksonville

GEORGIA

COLVIN, EMMETT D., Atlanta

ILLINOIS

COOLEY, WILLIAM, Peoria
 DAILY, EDWIN F., Chicago
 MALCOLM, WILLIAM A., Peoria
 SCHMITZ, HERBERT E., Chicago
 TUCKER, BEATRICE E., Chicago
 WHITACRE, FRANK EDWARD, Chicago

IOWA

CROWDER, ROY E., Sioux City
 RANDALL, J. H., Iowa City

KENTUCKY

BARRETT, A. B., Lexington

MASSACHUSETTS

BERLIN, MAURICE G., Boston
 FINKEL, HENRY S., Boston
 GWYNNE, SAMUEL C., Worcester

MICHIGAN

HUBER, CARL P., Ann Arbor
 KENNEDY, ROBERT B., Detroit
 KRETZSCHMAR, NORMAN R., Ann Arbor
 WHITE, MILO R., Detroit

NEW JERSEY

BINGHAM, ARTHUR W., East Orange
 D'ACIerno, PELLEGRINO A., UNION CITY
 WATERS, EDWARD G., Jersey City

NEW YORK

ALDRIDGE, ALBERT H., New York City
 BULLARD, EDWARD A., New York City
 CLARK, CHESTER E., Syracuse
 DAICHMAN, ISIDORE, Brooklyn
 DAVIN, EDWARD J., New York City
 DUNCAN, CAMERON, Brooklyn
 FEINER, DAVID, Brooklyn
 FINLEY, JOHN R., New York City
 FISCHER, HENRY S., Brooklyn
 FRIEDMAN, SAMUEL LOUIS, Brooklyn
 GOLDBLATT, MYRON E., New York City
 GREENE, HARRY J., Brooklyn
 HALPERIN, JACOB, Brooklyn
 HAWTHORNE, JULIAN, Rye
 HENNESSY, JAMES P., New York City
 HIRSCH, AARON, Brooklyn
 HUGHES, E. C., Syracuse

HURD, RALPH A., New York City
 JUDD, JOHN W., Ithaca
 KALDOR, JOSEPH, Brooklyn
 KAMINESTER, SANFORD, Brooklyn
 KLEEGMAN, SOPHIA J., New York City
 KLEIN, HYMAN, Brooklyn
 KRAUSHAR, SAMUEL, Brooklyn
 LOBSENZ, JACOB M., New York City
 LORBER, HERMAN, New York City
 McMANUS, JAMES P., Hollis, L. I.
 MALLIA, WILLIAM M., Schenectady
 MEAGHER, WILLIAM C., Brooklyn
 MERRIAM, MAXWELL S., Brooklyn
 MUELLER, CHARLES W., Brooklyn
 O'CONNOR, FRANCIS E., Kingston
 REID, GEORGIA, New York City
 ROGERS, JOHN F., Poughkeepsie
 ROSENBERG, MAXIMILIAN, Brooklyn
 SACKETT, NELSON B., New York City
 SALZBERG, ABRAHAM H., Brooklyn
 SCADRON, SAMUEL J., New York City
 SCHOENECK, F. J., Syracuse
 SHIELDS, FRANCES E., New York City
 SHIR, MARTIN M., Brooklyn
 WEINTRAUB, FREDERICK, Brooklyn
 WILSON, ROBERT A., Brooklyn
 WIMPFHEIMER, SEYMOUR, New York City
 WRANA, JOSEPH, Glendale, L. I.

NORTH CAROLINA

BRADFORD, WILLIAMSON Z., Charlotte
 HAMBLIN, E. C., Durham

OHIO

ABRAMS, S. B., Cleveland
 KENNEDY, EDWIN P., Cleveland
 ROBISHAW, ARTHUR W., Cleveland

PENNSYLVANIA

HEPP, JOSEPH A., Pittsburgh
 LAWS, GEORGE M., Philadelphia
 MILLER, FORD A., Philadelphia
 WILLIAMS, EDWARD F., Altoona

TENNESSEE

RUCH, WALTER ALLWEIN, Memphis

VIRGINIA

WILLIAMS, T. J., University

WISCONSIN

DARLING, FRANK E., JR., Milwaukee
 HORWITZ, JACOB, Milwaukee

ONTARIO

HARRIS, LOUIS J., Toronto

For application forms and any information regarding coming examinations for certification, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pa.

American Board of Obstetrics and Gynecology Examination

The next written examination and review of case histories of Group B applicants for certification by this Board will be held in various cities of the United States and Canada on Saturday, December 7, 1935.

Application blanks and booklet of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for this examination must be filed in this office not later than November 1, 1935.

On going to press we are informed of the death of Dr. Barton C. Hirst of Philadelphia. An extended obituary will appear in the October issue of the JOURNAL.

Books Received

BIRTH CONTROL. ITS USE AND MISUSE. By Dorothy Dunbar Bromley, with an introduction by Dr. Robert Latou Dickinson. 304 pages. Harper & Brothers, New York, 1934.

PARENTHOOD, DESIGN OR ACCIDENT? A Manual of Birth-Control. By Michael Fielding, M.D. With 8 illustrations, 239 pages. The Vanguard Press, New York, 1935.

LA ROENTGENTHERAPIE DES FIBROMYOMES DE L'UTERUS, ET DE METROPATHIES HEMORRAGIQUES. Par Paul Gibert. Avec 10 figures dans le texte. 110 pages. Masson et Cie, Editeurs, Paris, 1935.

ECONOMIC PROBLEMS OF MEDICINE. By A. C. Christie, M.S., M.D., Professor of Clinical Radiology, Georgetown University, Medical School, etc. 242 pages. The Macmillan Company, New York, 1935.

FACIES DOLOROSA. Das Schmerzliche Antlitz. Von Dr. H. Killian. Mit 64 Abbildungen, 88 pages. Verlag von Georg Thieme, Leipzig, 1934.

DER UNVERMUTET SCHNELLE TOD IN SCHWANGERSCHAFT, GEBURT UND WOCHENBETT. Von Geh. Med. Rat Professor Dr. Erwin Kehrler, Direktor der Univ. Frauenklinik in Marburg. 52 pages. Verlag von Ferdinand Enke, Stuttgart, 1934.

LUNGENTUBERKULOSE UND SCHWANGERSCHAFT. Von H. Braeuning, Chefarzt der Fuersorgenstelle fuer Lungenkranke in Stettin, etc. 275 pages. Mit 391 Kurven und Abbildungen. Verlag von Georg Thieme, Leipzig, 1935.

JEWISH CONTRIBUTIONS TO MEDICINE IN AMERICA (1656 to 1934). With medical chronology, bibliography and 69 illustrations. By Solomon R. Kagan, M.D. 549 pages. Published by Boston Medical Publishing Co., Boston, 1934.

CLINICAL MANAGEMENT OF SYPHILIS. By Alvin Russell Harnes, M.D., Chief of Congenital Luetic Clinic, New York Hospital. The Macmillan Company, New York, 1935.

AIDS TO SURGERY. By Cecil A. Joll, Senior Surgeon to the Royal Free Hospital, etc., and Reginald C. B. Ledlie, Surgeon to Miller General Hospital. Illustrated by H. H. Greenwood, Consulting Surgeon, G. W. R. Hospital, Swindon. Sixth edition, William Wood & Company, Baltimore, 1935.

PHYSIOLOGIE UND PATHOLOGIE DER WEHEN. Von Dr. Tassilo Antoine, Assistent der Univ. Frauenklinik, Professor Weibel, Wien. Mit 43 Kurven. Verlag von Wilhelm Maudrich, Wien, 1935.

DISEASES OF CHILDREN. Third edition with contributions by 36 authors; edited by Hugh Thursfield, physician, Hospital for Sick Children, etc., and Donald Paterson, physician to out-patients, Hospital for Sick Children, etc. William Wood & Company, Baltimore, 1934.

THE WOMAN ASKS THE DOCTOR. By Emil Novak, M.D., Associate in Gynecology, Johns Hopkins Medical School. Illustrated by Carl Clarke. Williams & Wilkins Company, Baltimore, 1935.